THE CANADIAN ANAESTHETISTS' SOCIETY JOURNAL

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JOURNAL DE LA SOCIÉTÉ CANADIENNE DES ANESTHÉSISTES

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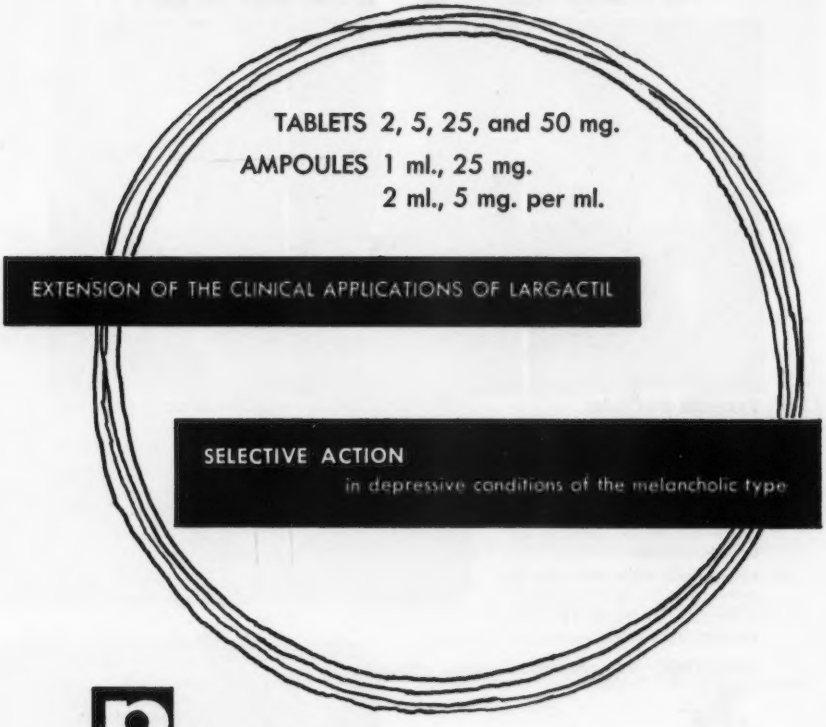
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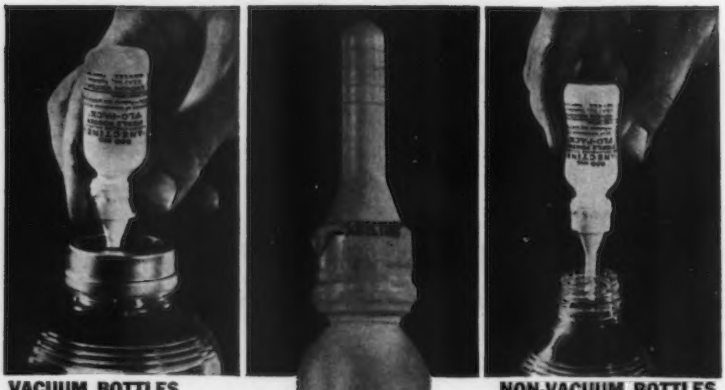

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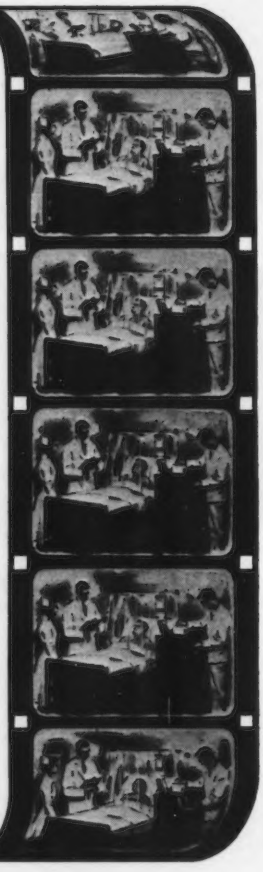

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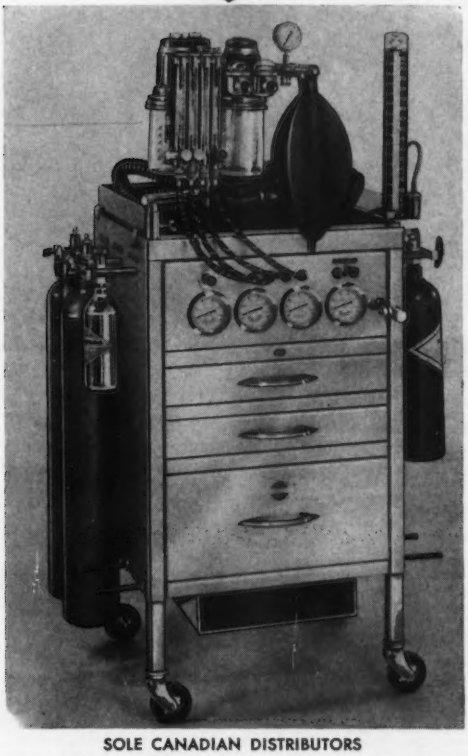

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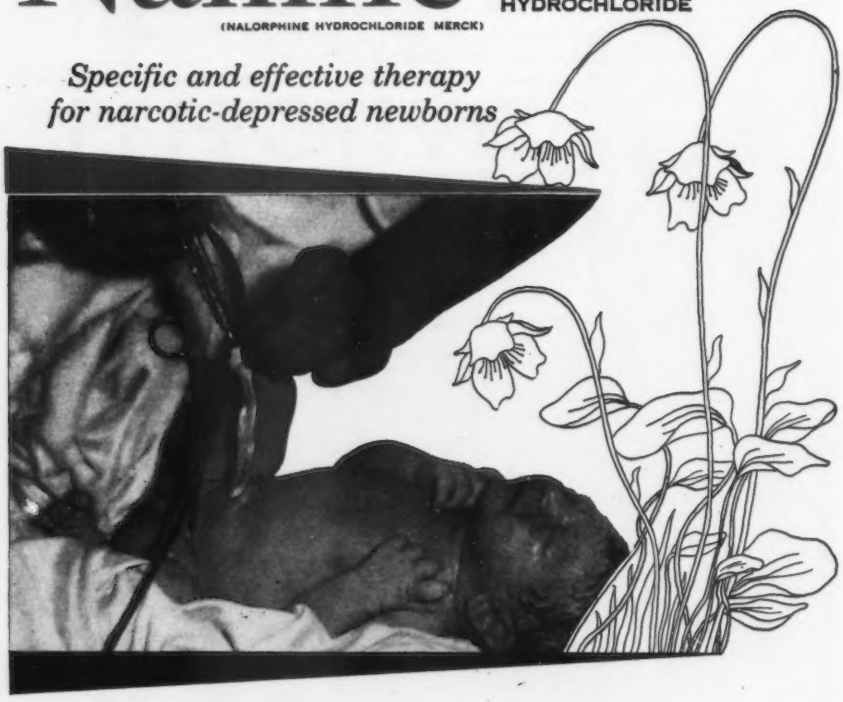

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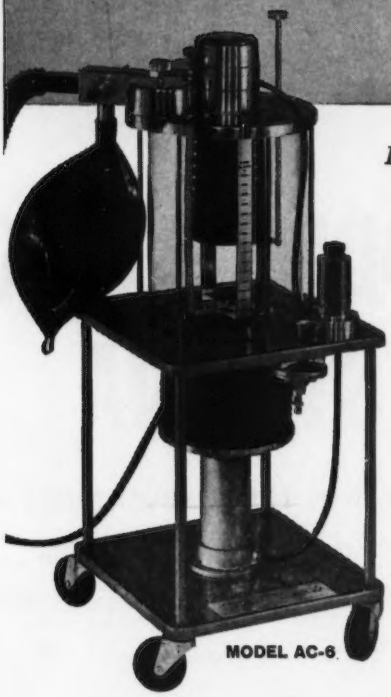

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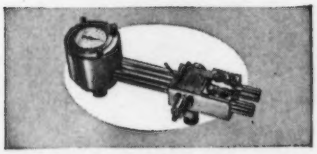

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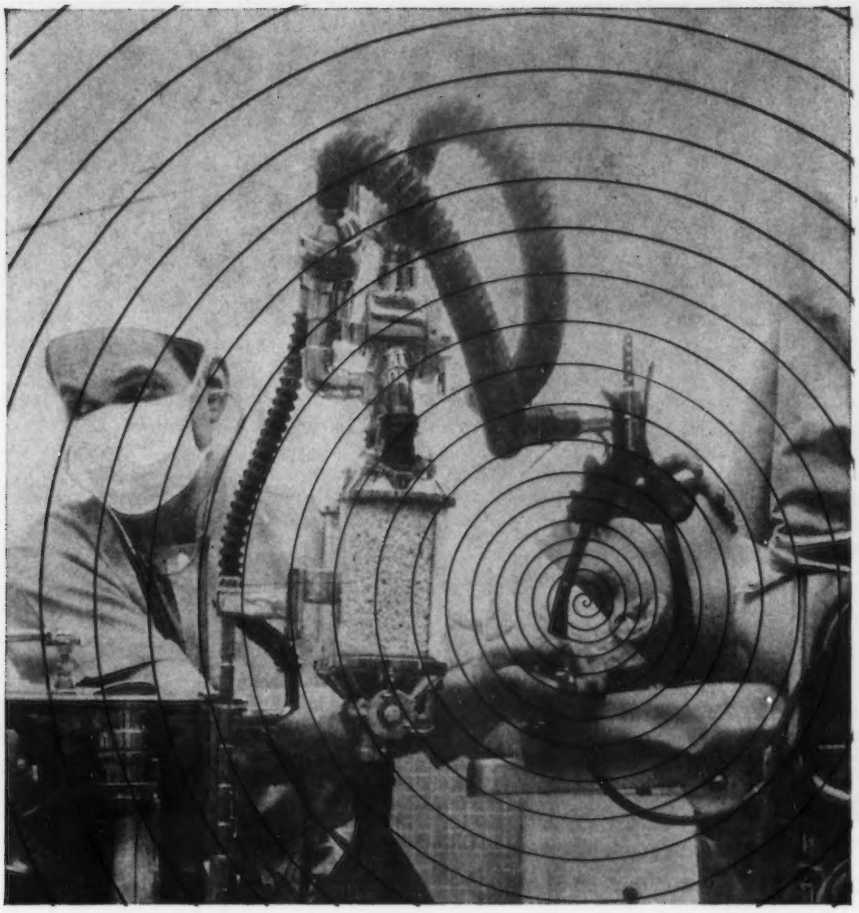

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ANAESTHETIC NEWS

The History of Anaesthesia

PART III *From Horace Wells to John Snow*

The development of anaesthesia has, like the history of so many other useful contributions to society, been filled with both hopes and disappointments. Fortunately, failure often showed the way to greater success.

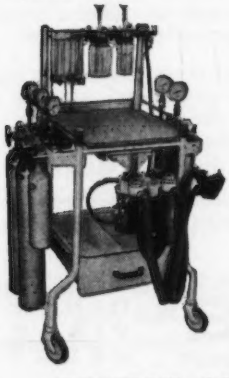
This was the case with Wells' tragic demonstration of nitrous oxide as an anaesthetic. He had addressed the assembly at Harvard Medical School and during the lecture administered gas to a boy and then extracted a tooth. Unfortunately the patient screamed in pain and Wells was hissed out of the room as a fraud. His failure, however, spurred William Morton into embarking on a study of the science, and although we now credit Morton with the introduction of ether as an anaesthetic agent, he was never in his lifetime officially recognized for this.

After his death his colleagues and friends in Boston erected a monument in his honour bearing the following inscription:

> William T. G. Morton
> Inventor and Revealer of Anaesthetic Inhalation. Before Whom, in All Time, Surgery was Agony. By Whom, Pain in Surgery was Averted and Annulled. Since Whom Science has Control of Pain.

When James Simpson of Edinburgh focussed medical attention on anaesthesia, he did it by advocating chloroform as the agent and he concentrated on relieving labour pains. His theory about chloroform was later acted upon by John Snow. Snow had practised anaesthesia in dentistry and surgery using an improved ether inhaler, but he abandoned this when Simpson's success with chloroform became known to him. He invented a new inhaler and administered chloroform to over 4,000 patients without a death occurring.

It was John Snow who acted as anaesthetist when Queen Victoria gave birth to her eighth child, Prince Leopold, in 1853. This incident finally silenced the outcries from the Church, and was undoubtedly the turning point in the fight for acceptance of anaesthesia. Since then, the medical profession has acknowledged its benefits, and suffering mankind the world over has sighed with heartfelt relief.



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References: 1. Sadove, M. S.: A preliminary report on Carbocaine, a new local anesthetic. Submitted for publication. 2. Luduena, F. P.; Hoppe, J. O.; Coulston, F., and Drobeck, H. P.: The pharmacology and toxicology of mepivacaine, a new local anesthetic, *Toxicol. & Appl. Pharmacol.* To be published. 3. Rovenstine, E. A.: Personal communication. 4. Young, J. A.: Upper arm block with Carbocaine (mepivacaine), a new anesthetic agent, *Anesth. & Analg.* To be published. 5. Griesser, Gerd: Erfahrungen mit einem neuen Lokalanestheticum, *Anaesthesist* 6:364, Oct., 1957.

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MEDICINE AND THE STATE

THE TENDENCY for politicians to meddle in the practice of medicine appears to be as old as recorded history. The archaeologists have provided us with details of the penalties imposed by the State on practitioners of ancient Babylon who failed to cure their patients. Today there is hardly a politician extant who does not publicly subscribe in some form to the creed that government can manage the provision of medical care better than the doctors.

With every political party in Canada looking to medical care as the next thing which may be given "free" in return for loyalty at the polls, it is time for the physician to make an effort to develop some clarity in his thinking in this matter—to know *what* he thinks, and *why*.

It is a great misfortune that some proponents of State-sponsored medical schemes seem to feel that they will gain their point by attacking the profession of medicine. The doctors are represented as "money grubbers," denying medical care to those unable to pay for it, growing fat on the misfortunes of others. Certainly all this sounds strange in a land which enjoys one of the highest standards of medical care in the world—where no one need lack for medical care who needs it, or who *thinks* he needs it, regardless of his ability to pay. Surely the least likely way to gain the sympathy and co-operation of the profession is to sneer at its ideals and besmirch its reputation. The doctor cannot be blamed under these circumstances if he begins his consideration of this problem with the firm conviction that the proponents of State medical schemes are not truly interested in the improvement of medical care, but only in selling more newspapers or buying more votes.

Undoubtedly there are many doctrinaire socialists who believe that everything can be done better by the State. Without the necessity of agreeing with their philosophies, one can at least respect them for their sincerity. These people and many less sincere are quite unable to understand the physician's opposition to State control of medical practice, because the professional attitudes of medicine are completely foreign to them. Physicians tend to forget that most of mankind works only to make a living, and that basically most men consider work as something distasteful which they would gladly avoid. This means that most of our society works *only* for money, and they fail completely to understand that the professional man can have any other motivation. By this reasoning, any opposition by the profession to the encroachment of third parties in the control of medical practice is interpreted as an attempt to preserve the monetary rewards of practice; and from this it follows in some minds that *if* the profession is so anxious to preserve the *status quo*, the incomes of doctors must be too high. Q.E.D.!

Any intelligent man who wishes to consider the facts dispassionately will be aware that the financial returns of the practice of medicine are not likely to change much because the physician's fee comes from the public rather than the private purse. What then are the doctors fighting about?

An elementary and serious error which is evident particularly in the daily press is the failure to distinguish between a health insurance plan, to which the state may contribute, and a *state-controlled* medical care plan, which must ultimately interfere with the physician's treatment of his patient. The primary interest of the medical profession is that the practitioner shall retain the freedom to provide for his patient the best care and the best treatment available. The best care and the best treatment mean that the best of equipment, drugs, and technical assistance must be available, and that there must be no deterrent to their use. These things cost money. Money spent to maintain an unnecessary administrative bureaucracy is no longer available to provide these essentials of good medical care—and governmental control and a *budget* for medical care means that administrative costs will have first call on the budget, and that the medical care of the community will be regulated by the amount of money which is left after this requirement is met. Experience elsewhere has shown that pressures are applied to the physician in order to balance the budget, which either make it impossible for him to give his patients the attention and care which they require and deserve, or influence his treatment of them.

No satisfactory solution to the divergence of views on this subject can be possible until the politicians and the press cease their ridiculous attacks on the attitude of physicians to the treatment of their patients, and make some attempt to understand the professional attitude. On the other hand, the public is not likely to come to understand the issue until the doctors stop talking ambiguously about the prospect of deterioration of medical service under government control, and begin to know and to say *exactly* what they mean. This is no matter for woolly thoughts and woolly words.

LA MEDECINE ET L'ETAT

LA TENDANCE qu'ont les politiciens de s'immiscer dans la pratique de la médecine nous semble aussi vieille que l'histoire elle-même. Les archéologues nous fournissent des détails sur les punitions imposées par l'état aux practiciens de l'ancienne Babylone qui ne réussissaient pas à guérir leurs malades. Aujourd'hui, rares sont les politiciens qui, publiquement, ne souscrivent pas sous quelque forme à l'assurance que le gouvernement peut organiser le paiement du coût des soins médicaux mieux que les médecins.

Etant donné que tous les partis politiques au Canada se retournent actuellement vers les soins médicaux comme étant la prochaine chose qu'ils aimeraient à donner gratuitement en reconnaissance d'un vote bien placé au bureau de votation, il est temps que le médecin fasse un effort pour clarifier ses idées sur ce sujet—qu'il sache ce qu'il pense et pourquoi il le pense.

Il est bien malheureux que les préconisateurs de plans de soins médicaux payés par l'état soient sous l'impression que c'est en attaquant la profession médicale qu'ils vont gagner leur point. Ils décrivent les médecins comme des assoiffés d'argent, refusant leurs soins à ceux qui ne peuvent pas payer et augmentant leur pécule au détriment des malheureux. Sans aucun doute, ces discours nous semblent un peu étranges dans un pays qui possède les plus hauts standards de soins médicaux dans l'univers, pays où quiconque a besoin de soins médicaux ou croit en avoir besoin peut en avoir, qu'il puisse ou non payer. Un des moyens les plus sûrs de s'aliéner la sympathie et la coopération de la profession est de se moquer de son idéal et de salir sa réputation. Peut-on blâmer le médecin, en de semblables circonstances, s'il aborde l'étude de ce problème avec la ferme conviction que les préconisateurs de plans d'assurance-santé ne sont nullement intéressés à améliorer les soins médicaux, mais plutôt à vendre plus de journaux et à acheter plus de votes.

Sans doute il existe plusieurs doctrines socialistes qui sont sous l'impression que, par l'état, tout peut être mieux fait. Sans accepter leur philosophie, nous pouvons toutefois les respecter à cause de leur sincérité. Ces gens et un grand nombre d'autres moins sincères sont tout à fait incapables de comprendre pourquoi le médecin s'oppose au contrôle de la pratique médicale par l'état, parce qu'ils ignorent tout des attitudes professionnelles de la médecine. Les médecins semblent oublier que la plupart des hommes ne travaillent que pour gagner leur vie et que, foncièrement, la majorité considère le travail comme une chose désagréable et sans attrait qu'elle serait bien contente de laisser tomber. Cela vient à dire la plus grande partie de notre société ne travaille que pour l'argent et on ne peut pas se mettre dans l'idée que le professionnel puisse avoir d'autres motifs d'action. En raisonnant ainsi, toute opposition de la part de la profession à l'empiètement d'un tiers dans le contrôle de la pratique médicale est interprétée

comme un désir de protéger les récompenses monétaires de la pratique médicale; puis, de cela, d'après certains, le raisonnement suivant découle: si la profession désire tellement que les choses ne changent pas, c'est que les revenus des médecins doivent être trop élevés!

Toute personne intelligente qui veut étudier les faits objectivement réalisera que les revenus économiques de la pratique médicale ne seront pas susceptibles de changer beaucoup parce que les honoraires médicaux seront payés à même les deniers publics plutôt qu'à même la bourse du particulier. Mais alors, pourquoi les médecins demeurent-ils opposés?

Une erreur élémentaire mais sérieuse que l'on rencontre particulièrement dans les journaux quotidiens, c'est le manque de distinction que l'on semble faire entre un plan d'assurance-santé auquel l'état peut contribuer et un plan pour soins médicaux contrôlé par l'état qui, en définitive, va intervenir dans le traitement du malade. Le principal intérêt de la profession médicale consiste en ce que le praticien demeure libre de prodiguer à son malade les meilleurs soins et les meilleurs traitements qu'il connaisse. Quand on dit: meilleurs soins et meilleurs traitements, cela signifie le meilleur outillage, les meilleurs médicaments, la meilleure assistance technique que l'on puisse souhaiter et surtout qu'il n'existe pas d'empêchement à leur emploi. Tout cela coûte de l'argent. Puis l'argent dépensé pour entretenir une bureaucratie administrative inutile ne peut plus servir à l'achat de ce choses essentielles aux bons soins médicaux; alors le contrôle gouvernemental et un budget pour les soins médicaux laissent entendre que les frais d'administration vont amputer le budget et que les soins médicaux de la population vont être soumis et proportionnels aux sommes d'argent qui resteront après les dépenses payées. Les expériences vécues à l'étranger nous apprennent qu'il s'exerce des pressions sur les médecins pour balancer le budget ce qui les place dans la situation ou bien de ne pas donner à leurs malades l'attention et les soins qu'ils requièrent et qu'ils méritent, ou bien d'influencer le coût des traitements à leur donner.

Nous ne voyons pas d'issue satisfaisante à cette divergence de vue sur ce sujet, à moins que les politiciens et la presse ne cessent leurs attaques ridicules sur l'attitude des médecins à l'égard des traitements à leurs malades et qu'ils ne fassent des efforts pour comprendre l'attitude professionnelle. D'autre part, le public ne parviendra pas à comprendre l'enjeu à moins que les médecins ne cessent de parler de façon ambigue sur la possibilité de détérioration du service médical sous le contrôle du gouvernement et qu'ils commencent à savoir et à dire exactement ce qu'ils pensent. Ce n'est pas le sujet ni le moment où il faudrait avoir des idées confuses exprimées en termes couverts.

THE DISCOVERY AND PHARMACOLOGY OF CYCLOPROPANE[1]

G. H. W. LUCAS[2]

IT WAS over thirty years ago, on November 22, 1928, that I prepared, in the laboratory of the Department of Pharmacology of the University of Toronto, the first sample of cyclopropane ever to be used for anaesthetic experiments on laboratory animals. I trust the reader will bear with me, however, if I first go back a few years prior to that date to show how previous research in the Department led to the discovery of cyclopropane. The data I shall present may be gleaned piecemeal from the various departmental publications prior to 1928, but hitherto no one has brought them together in one paper.

I first became acquainted with Professor Velyien E. Henderson, several years before I joined his Department, through my efforts to discover the growth-promoting factor in yeast, under Professor W. Lash Miller of the Department of Chemistry. Certain feeding experiments on animals were carried out in the Department of Pharmacology. Later I served as biochemist for the late Sir Frederick Banting, who had his laboratory in Professor Henderson's Department. Because of this I was aware of some of the research in progress in anaesthesia and when, in 1927, Professor Henderson offered me the opportunity of joining in this research, I accepted without hesitation.

The story from 1927 on involves four persons—the late Professor Velyien E. Henderson, Dr. W. Easson Brown, Mr. Allan Brock, and myself. Mr. Brock, who at the time was laboratory assistant and machinist in the Department, assisted in operations on the animals and in the design and manufacture of any new and essential apparatus.

At least 35 papers dealing with anaesthetics and anaesthesia have been published by members of the Staff in Pharmacology. A worldwide quest for a general anaesthetic more suitable than ether or chloroform or nitrous oxide reached its peak about 1923. The earliest investigations in this field were undertaken by Paul Bert in 1878 on nitrous oxide, but little attention had been paid to his results.

Ethylene was under serious investigation in various laboratories on the North American continent about 1920, and in Toronto, Dr. W. Easson Brown became interested in it. He was aware that in 72 per cent concentration it was not toxic to animals; in August, 1922, he anaesthetized rabbits and mice with 80 per cent ethylene and 20 per cent oxygen. A paper on this subject, which he read before the Toronto Academy of Medicine on February 20, 1923, was published in the March 7 issue of the *Canadian Medical Association Journal* of that year (1). A week later A. B. Luckhardt and J. B. Carter published a report of their work on the same gas in the *Journal of the American Medical Association* (2). In a later

[1]Presented at the Annual Meeting, Canadian Anaesthetists' Society, May 6, 1959.

[2]Department of Pharmacology, University of Toronto.

publication, on May 19 of the same year, they reported that they had conducted 106 operations in hospitals, using this gas as a general anaesthetic. In the American literature, Brown is not given credit for the earliest publication on the anaesthetic value of ethylene in laboratory animals, possibly because he published his results in a Canadian journal.

Brown meanwhile continued his experimental work on animals in co-operation with Dr. Henderson and extended it to include anaesthetization of some members of the laboratory staff. He used it in several operations on human patients. The fact that ethylene could be used in concentrations of 80 per cent or over for satisfactory anaesthesia, and had been used extensively by Luckhardt, did not satisfy Dr. Brown and Professor Henderson. From the study of the narcotic properties of alcohol, it was postulated that propylene would be a more potent gas than ethylene and its preparation was begun in the laboratory early in 1924. In July of that year Brown reported in the *Journal of Pharmacology and Experimental Therapeutics* (3) that propylene had definite anaesthetic properties and would induce anaesthesia in concentrations as low as 37 per cent in air or oxygen. Anaesthesia, he asserted, could be maintained in concentrations from 20 to 31 per cent in oxygen; in concentrations of 65 per cent or over it was considered toxic.

A chemical engineer, Mr. L. J. Bonham, working on a special grant in the Department of Pharmacology, succeeded in making a very pure sample of propylene and reported his findings in the February, 1925, issue of the *Journal of the American Pharmaceutical Association* (4). Samples of the gas thus made were excellent for anaesthesia on experimental animals. However, when it was tanked in steel alloy tanks, toxic materials developed in it; these were not present in the original gas prepared in the laboratory. As no means were found to account for this unexpected toxic action, or to remove the toxic product, anaesthetic research with this gas came to a standstill.

It was at this juncture that I joined the staff of the Department of Pharmacology. As I reviewed the literature on anaesthesia and became more familiar with the work of Brown and Henderson on propylene, it was apparent that the serious metabolic changes occurring during anaesthesia were in part due to anoxaemia. We decided to direct our attention to the work of Paul Bert (5) on nitrous oxide administered with oxygen under pressure. He had maintained that satisfactory anaesthesia could be attained with nitrous oxide–oxygen mixtures under pressure greater than that of the atmosphere. He pointed out that, by increasing the pressure to $1\frac{1}{4}$ atmospheres in a nitrous oxide 80 per cent–oxygen 20 per cent mixture, the partial pressures of the nitrous oxide would be the same as that of pure nitrous oxide. According to Henry's Law of the solution of gases, a patient breathing this mixture under pressure would have in his blood as much nitrous oxide as he would have when he breathed pure nitrous oxide. Bert reported successful surgery with this anaesthetic mixture.

Over a year was spent investigating the anaesthetic value of nitrous oxide–oxygen mixtures under pressure. We experienced much difficulty in designing a suitable tank in which to anaesthetize laboratory animals (rabbits, cats, and rats). After several tanks burst under pressure, a satisfactory one was made from steel tubing heavily reinforced.

Despite the fact that pressures up to 2 atmospheres were employed and partial pressures of nitrous oxide were 1½ times that of pure nitrous oxide when inhaled, a satisfactory state of deep surgical anaesthesia was not reached. Animals when stimulated could move about in the cage. Anaesthesia could be secured at these high partial pressures of nitrous oxide only when the partial pressure of oxygen was so low that anoxaemia was present.[3] Thus ended another anaesthetic venture. We seemed to have come to a dead end.

During the researches on nitrous oxide and oxygen under pressure, little attention had been paid to the tank of propylene, prepared by E. R. Squibb and Sons several years previously, which had developed peculiar toxic products. Professor Henderson now drew my attention to this unsuccessful experiment and suggested that I give the matter some attention to learn, if possible, what substance could have formed in the tanked gas. While searching the literature, I found that cyclopropane, which is an isomer of propylene, might be formed during any chemical reaction in which propylene was prepared. I performed some qualitative analyses on the sample of toxic gas and came to the conclusion that some cyclopropane was present. I suggested that this gas might be the toxic material; I could not find any data in the literature regarding its toxic effects when inhaled. Professor Henderson therefore decided that I should prepare cyclopropane, employing the method published by Wilstätter in which trimethylenebromide was reduced by zinc to cyclopropane in the presence of alcohol and traces of water. Since we suspected the gas was poisonous, it was approached with a great deal of care.

According to my notebook, the first sample of cyclopropane was prepared for anaesthesia on November 22, 1928 (Fig. 1). It was employed to anaesthetize cats in a manner similar to that used for propylene. Needless to say, the stage was set for anaesthetic experiments on this gas because much apparatus had been designed for research on ethylene and propylene. To our amazement, the cyclopropane was not toxic but anaesthetized animals in concentrations lower than those observed for any other anaesthetic gas. The animals recovered rapidly. It was evident that cyclopropane was a gas which invited further investigation.

I shall not burden you with minor details of the ensuing experiments. However, it is interesting to note that, as cyclopropane was soluble in sulphuric acid, it was relatively easy to measure concentrations in any mixture employed for anaesthesia. An impurity in the gas, probably saturated hydrocarbons, was obtained in quantity by dissolving out the cyclopropane in sulphuric acid and leaving this gas as a residue. When this residue was tested, it had no anaesthetic value. Experiments with cyclopropane showed that it was anaesthetic in a concentration of approximately 12 per cent in oxygen and that the concentration could be increased up to 30 per cent or so without causing serious toxic effects on the heart, but respiration at higher concentrations was somewhat shallow. Repeated administration of the gas to animals did not cause toxic effects (7, 8). The changes in metabolism were measured; these were practically nil. The gas was

[3]Although these results were published in the *Journal of Pharmacology and Experimental Therapeutics* in August, 1927 (6), some textbooks still state that nitrous oxide–oxygen mixtures under pressure give satisfactory anaesthesia.

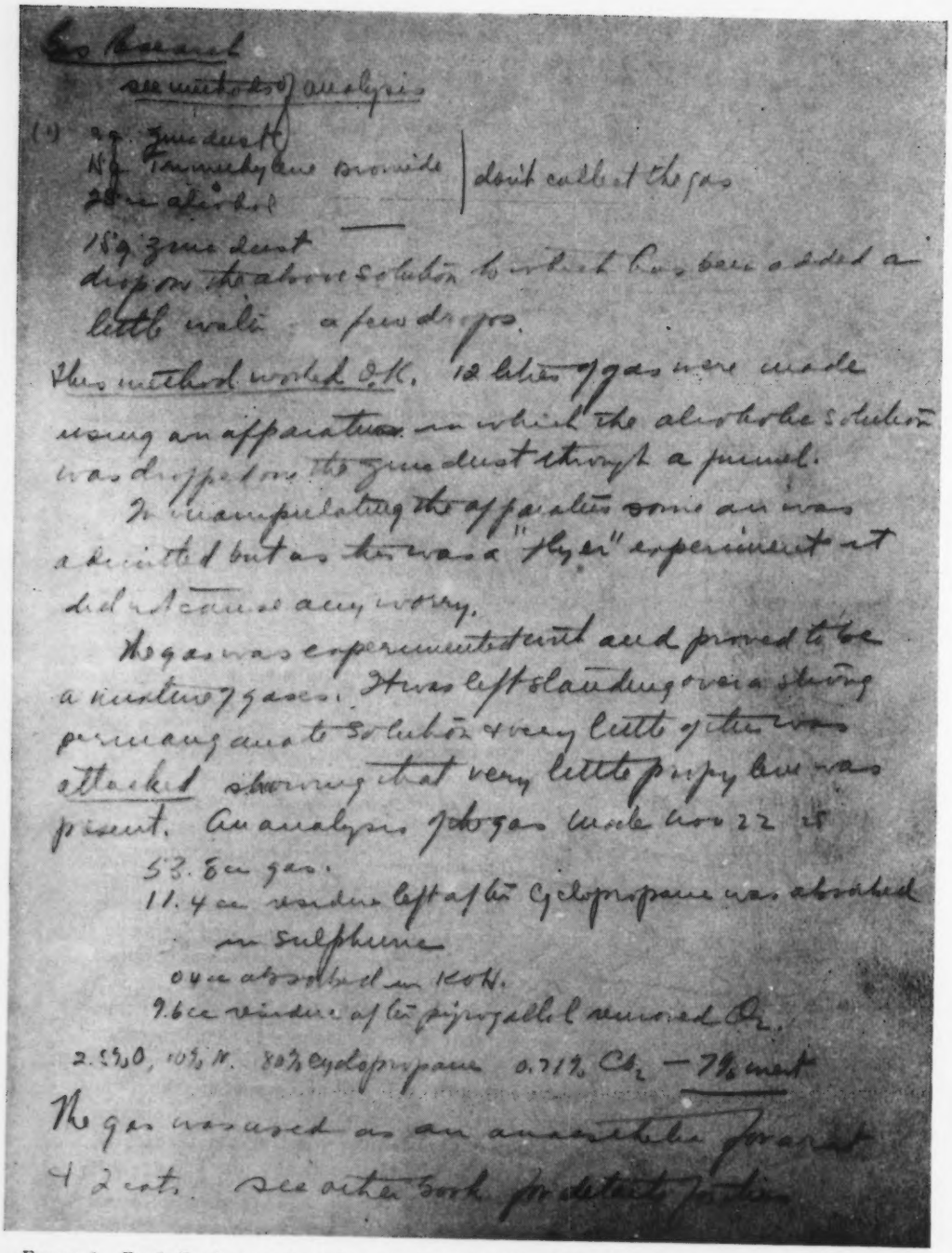

Geo Research
see methods of analysis
(1) 2g. Zinc dust
No Tannic hydrobromide | don't collect the gas
28cc alcohol
18g Zinc dust
drop on the above solution to which has been added a little water a few drops.
This method worked O.K. 12 litres of gas were made using an apparatus in which the alcoholic solution was dropped on the zinc dust through a funnel.
In manipulating the apparatus some air was admitted but as this was a "flyer" experiment it did not cause any worry.
The gas was experimented with and proved to be a mixture of gases. It was left standing over a strong permanganate solution & very little of it was attacked showing that very little propylene was present. An analysis of the gas made gave 22 cc
53.8 cc gas.
11.4 cc residue left after Cyclopropane was absorbed in sulphuric
0.4 cc absorbed in KOH.
9.6 cc residue after pyrogallol removed O_2.
2.5% O, 10% N. 80% Cyclopropane 0.7% CO_2 — 7% mist
The gas was used as an anaesthetic for about 4 or 5 cats. See other book for details further

FIGURE 1. Facsimile of a page from the author's notebook describing the first preparation of cyclopropane for anaesthetic purposes on November 22, 1928.

found to be explosive in air or in oxygen in anaesthetic concentrations; the oil-water partition coefficient was determined for it.

Professor Henderson reported briefly the results of our discovery at the Annual Meeting of the Canadian Medical Association, June 21, 1929 (9), and in October of the same year I presented a longer paper at the Annual Congress of Anaesthetists in Chicago (10). At that time we had not experimented on humans because we felt the gas was too impure.

The gas was subsequently prepared in pure state and the crucial test was performed, namely, tanking it under pressure in steel alloy tanks to ascertain whether or not impurities formed in the gas as they did with propylene. About 120 L. of gas were manufactured, purified, and then liquefied by being passed through a glass cooling coil immersed in liquid air. A small steel tank fitted with a connection for an anaesthetic machine and with a small removable plug was also cooled in liquid air (Fig. 2). The liquid cyclopropane was poured into the steel tank and the plug was inserted and secured. The tank was then permitted to remain in the laboratory at room temperature for about one month. As experiments on animals showed that the gas had not become toxic on standing, we proceeded to the experiments on humans.

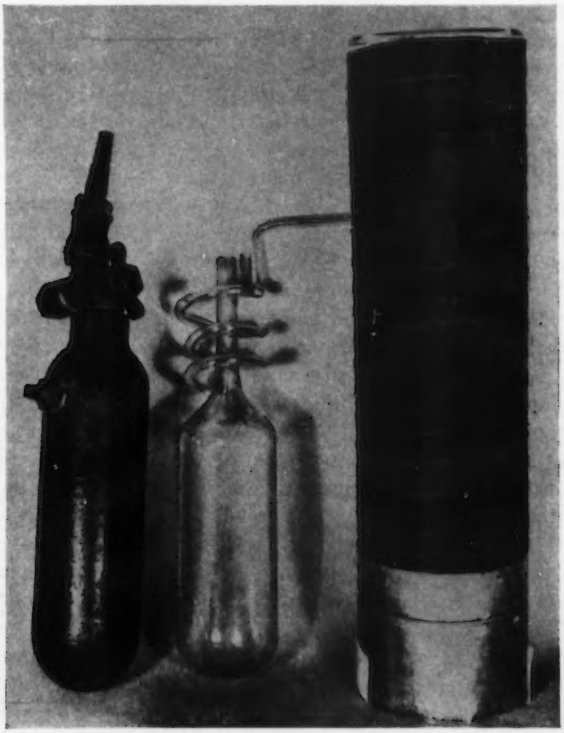


FIGURE 2. The equipment first used to liquify and the first tank used to contain cyclopropane for anaesthetic purposes.

Dr. W. Easson Brown had not been actively engaged in research on cyclopropane up to this date; he had discussed the experiments with Professor Henderson and me and we had agreed that his contribution would be mainly in the human experimentation. He was the first doctor in the world to administer cyclopropane in anaesthetic concentrations to humans, the first patient being Professor Velyien E. Henderson. At this first sitting, my task, as the analyst, was to check concentrations of the administered cyclopropane rapidly. Mr. Brock regulated the flow of gas and Dr. Brown looked after his patient. Both induction and recovery were rapid following a short anaesthetic. No ill effects followed. Dr. Brown then anaesthetized several members of the staff, myself included. We knew then that the gas was ready for experimental use in the hospital; we had at hand all the necessary equipment for measuring and controlling the anaesthetic concentrations.

At this particular time our luck changed. Three deaths which had occurred in Toronto in a relatively short period from the administration of ethyl chloride to patients gave rise to considerable newspaper publicity. Dr. Brown, who was on the anaesthetic staff of the Toronto General Hospital, begged the privilege of administering some of our sample of non-toxic cyclopropane to a patient, even for a short surgical procedure. A demonstration was put on one evening in our laboratory when Dr. Brown anaesthetized Dr. Frederick Banting before a number of physicians, but this was of no avail. Dr. Samuel Johnston, Head of the Department of Anaesthesia, who was present, observed the effects of cyclopropane, but in view of the unfortunate ethyl chloride deaths he forbade the use of cyclopropane in the hospital. It remained for others at a later date to investigate the anaesthetic value of this gas in surgery.

In Toronto we experimented with laboratory animals using commercial cyclopropane supplied by E. R. Squibb and Sons (Fig. 3) and then turned our attention to cyclopropane derivatives, hoping to discover one which would be an ideal liquid anaesthetic at room temperature, would have a boiling point about that of chloroform and could be administered by means of a mask. I prepared several chlor-derivatives of cyclopropane and also ethyl- and methyl-derivatives. None of these, however, to my mind was of value. Either they were too toxic or the boiling point was too high. I decided to abandon research in anaesthesia.

Professor Henderson continued a more extensive study of cyclopropane derivatives but found nothing of anaesthetic value. A chemist, Mr. A. H. R. Smith (11), was engaged to investigate the old tanked propylene and discovered hexenes in it; these were extremely toxic to laboratory animals. It would appear that Professor Henderson persevered until he had established the toxic component of the tanked propylene. It was fortunate for both of us that, when we began our experiments in 1928, I had come to the conclusion that cyclopropane was a constituent of the tanked propylene.

The stage for further cyclopropane experimentation was now moved to Wisconsin. Dr. Ralph M. Waters, in the Wisconsin General Hospital at Madison, had heard my paper on cyclopropane in Chicago and was very interested in the new anaesthetic. He and Professor Henderson were close friends and judging by a letter written to Professor Henderson in August, 1930, Professor Henderson

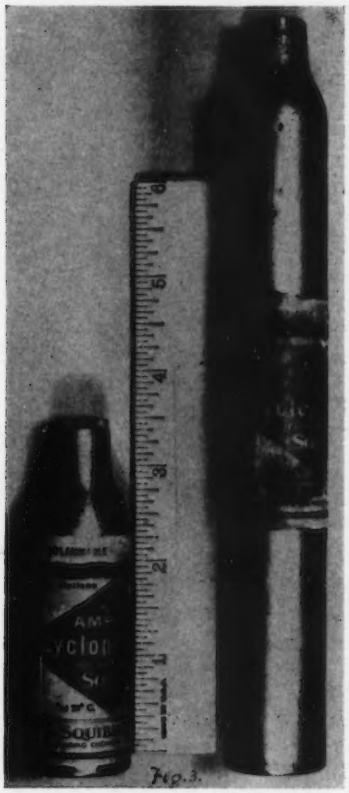


FIGURE 3. The first commercial "tanks" of cyclopropane supplied by E. R. Squibb & Sons.

must have encouraged Dr. Waters to use cyclopropane as an anaesthetic on patients, following our failure to try it in the Toronto General Hospital. After Professor Henderson's death I was asked to examine departmental files and records and discovered Dr. Waters' letter to Professor Henderson dated August 20, 1930 (Fig. 4). In this letter he stated that he had secured a small tank of cyclopropane from the Ohio Chemical Company and, after testing it on a dog, he had used it in the hospital on three patients. One operation was a simple appendectomy (35 min.; Fig. 5); one an inguinal hernia (40 min.; Fig. 6); a third on a fat woman, her tenth operation, for the removal of a gall bladder previously drained and the repair of a recurrent inguinal hernia (1 hr. 28 min.; Fig. 7). Dr. Waters had included a copy of the operating room charts for each patient. Analysis showed that about 40 per cent cyclopropane was essential for anaesthesia.

He states in his letter, "I believe that further investigations on this are distinctly indicated because the thing which anaesthesia needs more than anything

THE UNIVERSITY OF WISCONSIN
STATE OF WISCONSIN GENERAL HOSPITAL
MADISON

DIVISION OF SURGERY

August 20, 1930

Professor V. E. Henderson
University of Toronto
Ontario, Canada

Dear Doctor Henderson:

At your suggestion, I secured from the Ohio Chemical Company a small tank containing ten gallons of Cyclopropane. This, by means of the absorber technique, I found sufficient to anesthetise one dog, forty minutes, and being then satisfied that I need not harm the patients, I have used the remainder of the tank for three complete clinical anesthesias. One simple appendectomy--thirty-five minutes, one inguinal hernia--forty minutes, and one fat lady (her tenth operation) for the removal of a gall bladder, previously drained, and the repair of a recurrent inguinal hernia, the latter operation lasting one hour and twenty-eight minutes. An attempt to use the tank again this morning gave me an induction, but during the insertion of the pharyngeal airway, the small amount of cyclopropane was lost so that the one dog anesthesia and three clinical were all I could secure from ten gallons.

The gall bladder case described above was distinctly obese, and of the type most difficult to relax with any other method than spinal, and I believe that the results, so far as relaxation goes, were better than could have been secured in any other way than spinal. Whether it was as good as we would have secured with spinal, I doubt. The first case, appendectomy, was the type of individual in whom I would expect postoperative disturbances, a young Jewess, who had had some vomiting previous to operation. She vomited more than we would have expected postoperatively and complained of a "dizziness". The hernia case also vomited, although not excessively. The gall bladder and hernia were done this morning.

The blood pressure variations as a result of this agent, observed in three cases, were suprisingly stable it seems to me. I am asking my secretary to make copies of the operating room charts of these three cases for your information. The pulse rate in the first case was quite variable, but was extremely rapid before the anesthesia was begun due, I presume, to fright. There was a suprising lack of respiratory stimulation even during induction in the first case and we therefore didn't insert the soda lime during induction in the other two. The pulse in each case showed a slight irregularity when too great a concentration was reached, with some tendency to arhythmia, but the arhythmia was used by me as an indication for more oxygen. We made gas analyses of the oxygen-carbon dioxide content of bag at the end of each operation, and in the case of the hernia, did so as soon as anesthesia was well established. These gas analyses are at extreme variance with your laboratory results, and it is for this reason I am sending you them today. The first two cases, as you will see, were run on percentages in excess of 40 of cyclopropane. The gall bladder-hernia case had 23% cyclopropane at the end of operation it is true, but during the gall bladder procedure, I am sure the concentration was very much higher. We estimated that a 50-50 mixture was placed in the bag at the beginning and that it was replaced with a 40-60 mixture at the time the abdomen was opened.

FIGURE 4. Facsimile of a letter from Dr. Ralph Waters to Professor V. E. Henderson concerning the first use of cyclopropane in clinical surgery.

A constant delivery of oxygen, probably more than sufficient to cover the metabolic demand for oxygen was flowing throughout most of the operative time, so that the 23% found in the bag at the end of the hernia operation was probably much weaker than that used at the height of the operative procedure. I shall be glad to have your reaction to my discrepancies in cyclopropane concentrations as compared to your experience. We tried the addition of decidely more oxygen with the idea of dropping back to such percentages as you had found necessary in animals, but retching resulted when we did so. I regret having been unable to complete more clinical cases with the gas supplied me, and in case any more is manufactured, I should be very glad to give the gas a further trial clinically. The Ohio Chemical Company stated that they might make up more of the gas late in the fall. This ten gallons was all they had at the present time.

I believe that further investigations in this gas is distinctly indicated because the thing which anesthesia needs more than any thing else at the present time, it seems to me, is a quick acting gaseous agent which will produce reasonably extreme relaxation of abdominal muscles with reasonably rapid recovery therefrom. This, it seems to me, cyclopropane shows some possible evidence of doing.

Trusting that my notes may be of some interest to you, and with kindest personal regards, I am,

Sincerely,

Ralph Waters

Ralph M. Waters, M. D.
Department of Anesthesia

RMW:VH

FIGURE 4 (*continued*)

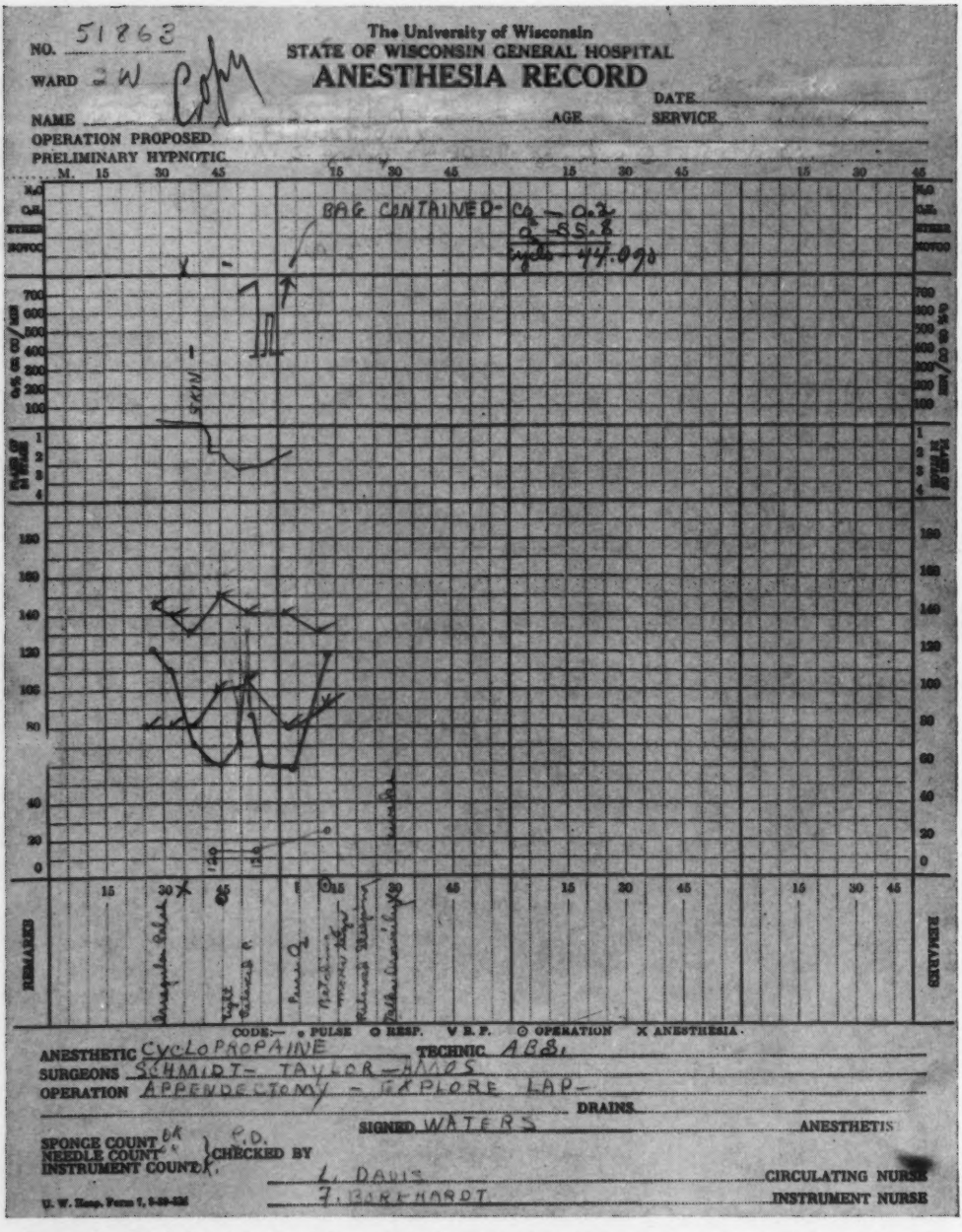


FIGURE 5. Facsimile of a copy of the anaesthetic record of the first patient anaesthetized with cyclopropane for a surgical operation, supplied by Dr. Waters to Professor Henderson.

PREOPERATIVE NOTES

NAME .....

Specific Toxemia ____
Hyperpyrexia ____
Hypermentation ____
Hypersthenic ____

SEX 7, AGE 22, WT. 110, HT. ..... COMPLEXION .....

AIRWAY ....., MOUTH .....

T. P. R. RATE 99.6-88-24, VITAL CAPACITY ....., BREATH H. ....., B. M. R.

LUNGS Ok.

HEART Ok. B. P. { Before B. H. ..... After B. H. .....

Hypometabolic ____
Hyposthenic ____

BLOOD: HB. 72, R. B. C. 5,800, W. B. C. 9,200, COAG. TIME .....

N. P. N. ....., CHLORIDES ....., SUGAR .....

Habitual Drugs ....

URINALYSIS Ok.

MISCELLANEOUS Cardiac Heart. DIAGNOSIS: CHRONIC APPENDICITIS

ANESTHETIC HISTORY AND CHOLITIS

PROPOSED OPERATION APPENDECTOMY

EVALUATION: PRESSURE RATIO ....., SHOCK INDEX .....,

ENERGY INDEX ....., CORNELL TEST ....., McINTYRE TEST ..... RISK { A ____ B ____ C ____ D ____

POST OPERATIVE NOTES: VOMITED SOME - COMPLAINED OF DIZZINESS HEADACHE NEXT DAY. GAS PAINS UNTIL THIRD NIGHT WHEN SHE SLEPT WELL. T. P. R. - NOT UNUSUAL POST OP.

FINAL COMMENT: .....

SIGNED ..... ANESTHETIST.

FIGURE 5 (*continued*)

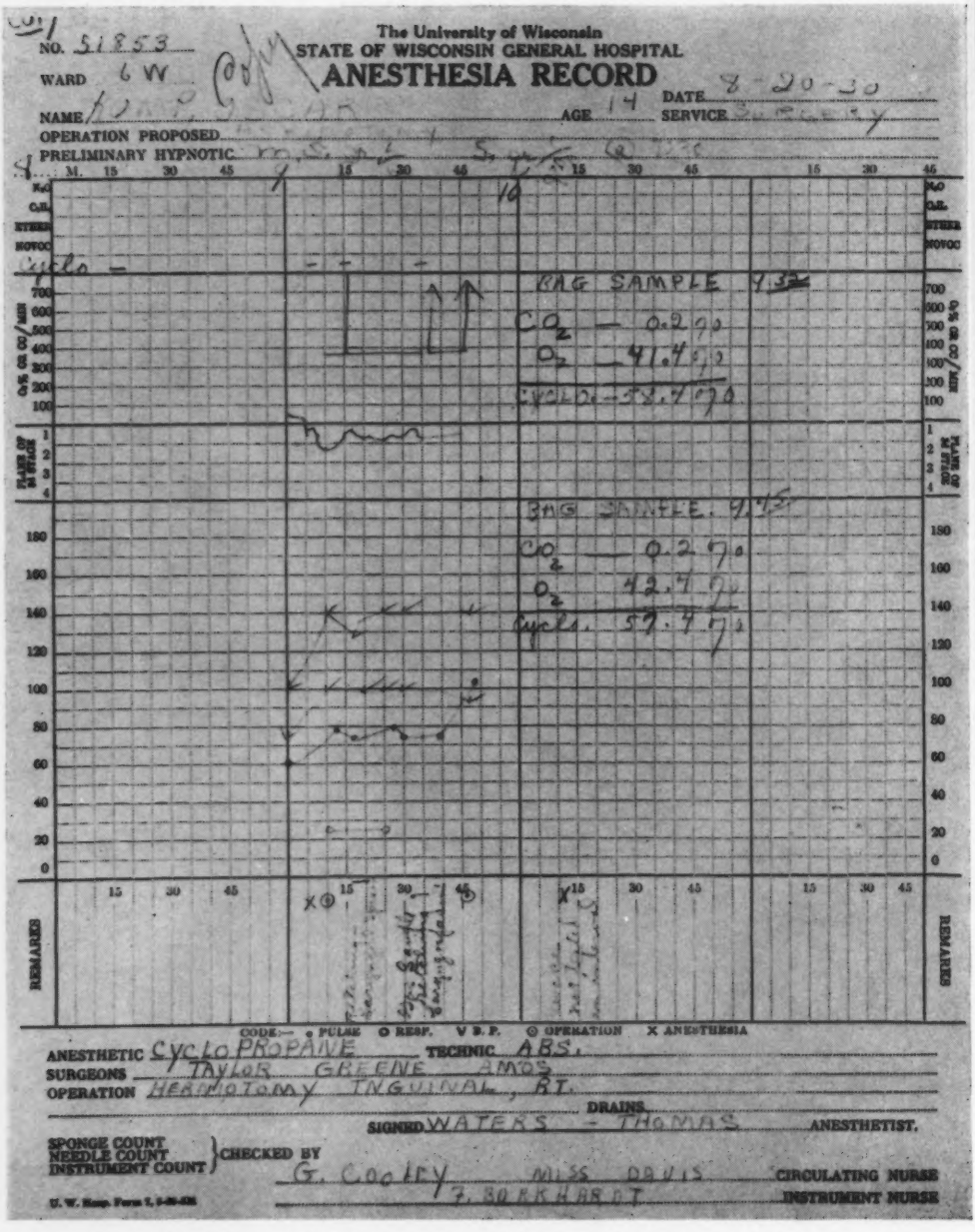
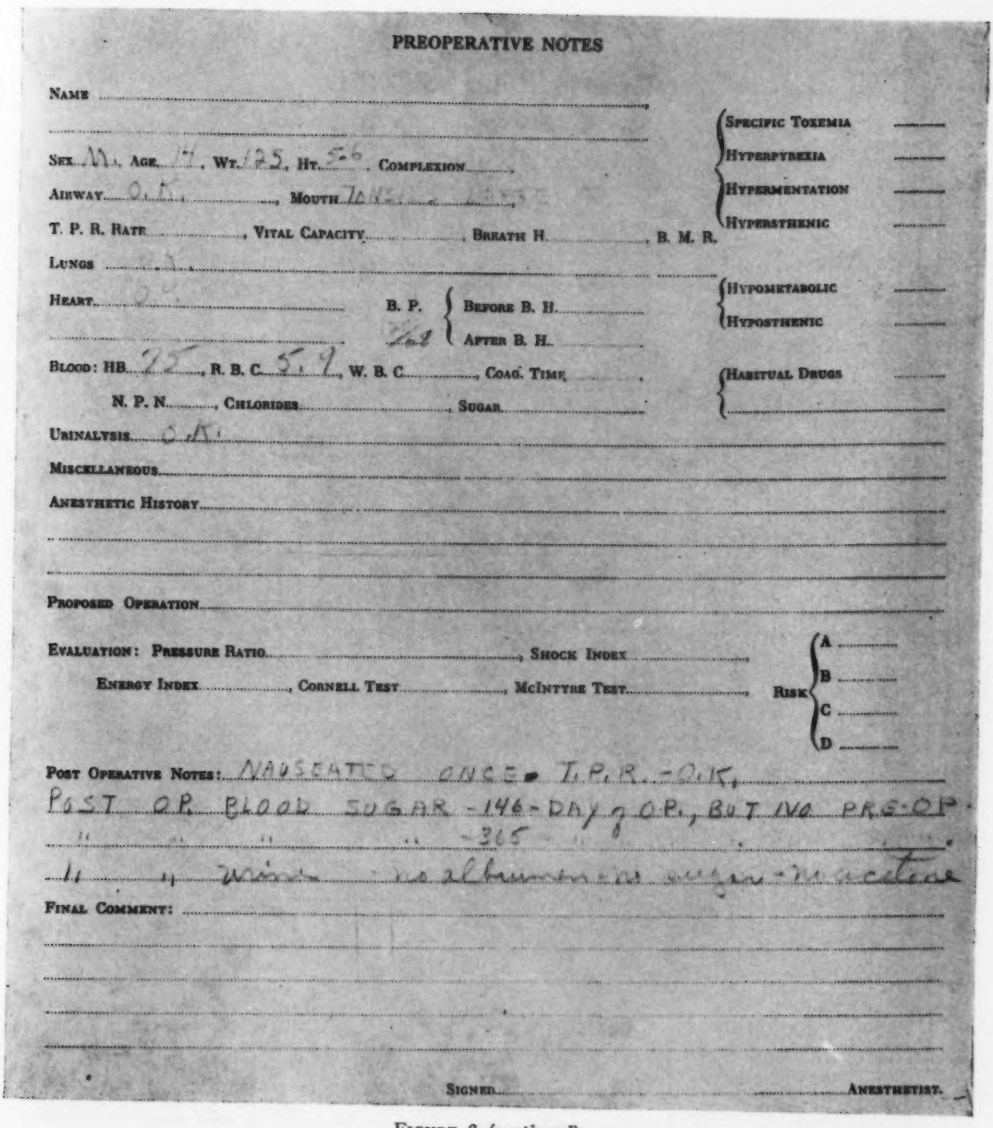


FIGURE 6. Facsimile of a copy of the anaesthetic record of the second patient anaesthetized with cyclopropane for a surgical operation, supplied by Dr. Waters to Professor Henderson.



PREOPERATIVE NOTES

NAME .....

SEX M. AGE 17, WT. 125, HT. 5-6, COMPLEXION .....

AIRWAY O.K., MOUTH O.K.

T. P. R. RATE ....., VITAL CAPACITY ....., BREATH H. ....., B. M. R. .....

LUNGS .....

HEART .....

B. P. { BEFORE B. H. ..... / 70 / AFTER B. H. .....

BLOOD: HB. 75, R. B. C. 5.9, W. B. C. ....., COAG. TIME .....

N. P. N. ....., CHLORIDES ....., SUGAR .....

URINALYSIS O.K.

MISCELLANEOUS .....

ANESTHETIC HISTORY .....

PROPOSED OPERATION .....

EVALUATION: PRESSURE RATIO ....., SHOCK INDEX .....

ENERGY INDEX ....., CORNELL TEST ....., McINTYRE TEST .....

SPECIFIC TOXEMIA .....
HYPERPYREXIA .....
HYPERMENTATION .....
HYPERSTHENIC .....
HYPOMETABOLIC .....
HYPOSTHENIC .....
HABITUAL DRUGS .....

RISK { A ..... B ..... C ..... D .....

POST OPERATIVE NOTES: NAUSEATED ONCE. T. P. R. - O.K.
POST OP. BLOOD SUGAR - 146 - DAY of O.P., BUT IVA PRE-OP.
" " " " - 365 " " "
" " " " - no albumen - no sugar - no acetone

FINAL COMMENT: .....

SIGNED ..... ANESTHETIST.

FIGURE 6 (*continued*)

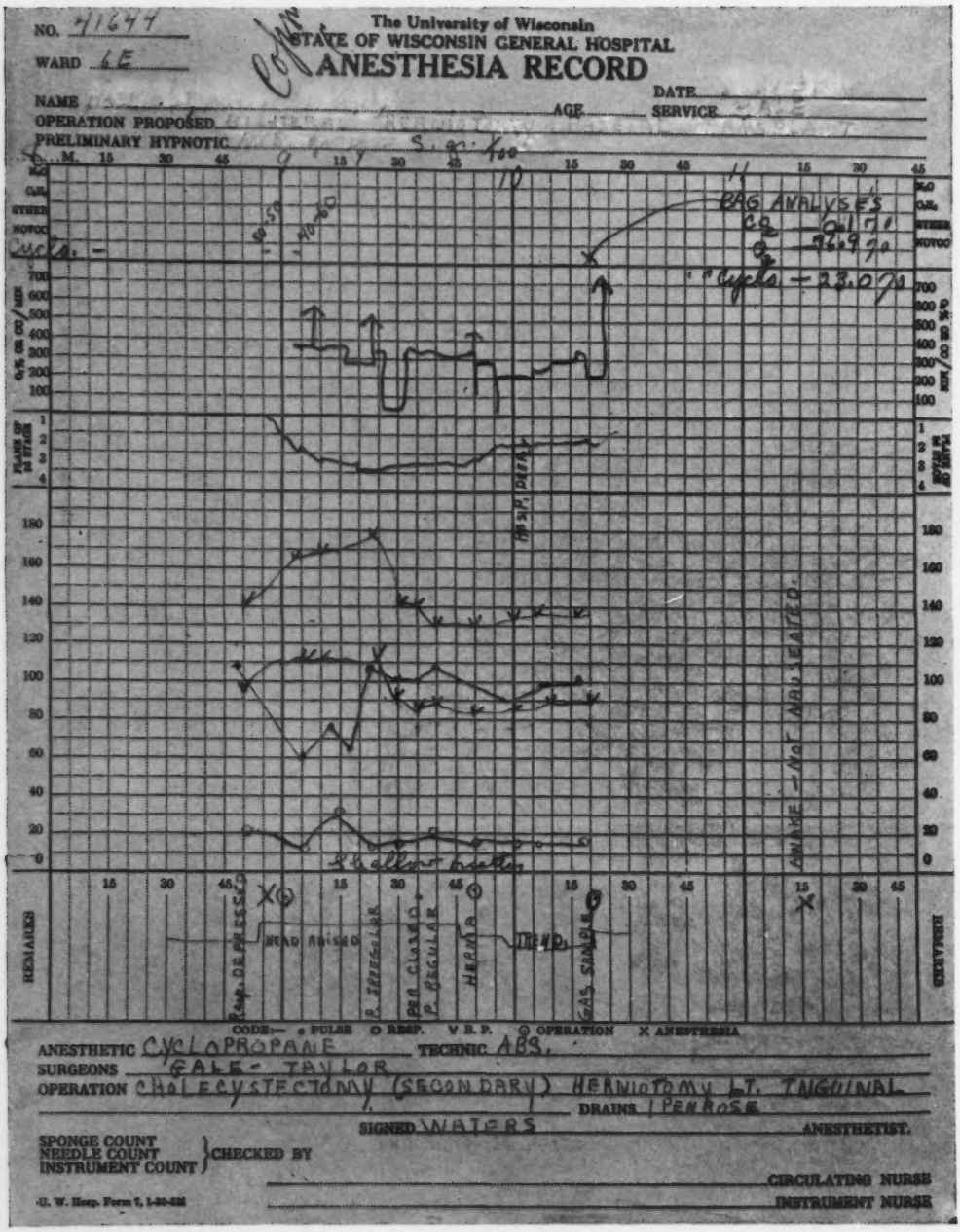


FIGURE 7. Facsimile of anaesthetic record of the third patient anaesthetized with cyclopropane, supplied by Dr. Waters to Professor Henderson.

PREOPERATIVE NOTES

NAME _____

SEX 7 AGE 45 WT. 161 HT. 5'4 COMPLEXION _____

AIRWAY O.K. MOUTH O.K.

T. P. R. RATE _____ VITAL CAPACITY _____ BREATH H. _____ B. M. R. _____

LUNGS O.K.

HEART O.K. B. P. 90/65 { BEFORE B. H. _____ AFTER B. H. _____

BLOOD: HB. 68 R. B. C. 5,280 W. B. C. 11,550 COAG. TIME _____

N. P. N. _____ CHLORIDES _____ SUGAR 98 - (8-19-30)

URINALYSIS Negative

MISCELLANEOUS OBESE, SLIGHT COLD

ANESTHETIC HISTORY Multiple previous operations to the hernial repairs and Cholecystotomy.

PROPOSED OPERATION Cholecystectomy and Herniotomy

EVALUATION: PRESSURE RATIO _____ SHOCK INDEX _____

ENERGY INDEX _____ CORNELL TEST _____ McINTYRE TEST _____

SPECIFIC TOXEMIA _____
HYPERPYREXIA _____
HYPERMENTATION _____
HYPERSTHENIC _____

HYPOMETABOLIC _____
HYPOSTHENIC _____

HABITUAL DRUGS _____

RISK A _____ B _____ C _____ D _____

POST OPERATIVE NOTES: NAUSEA AND VOMITING 5 TIMES IN 1ST 24 HRS. PERIODIC SLIGHT DYSPNOEA

URINE NEXT DAY TRACE OF ALBUMEN, NO SUGAR NOR ACETONE.

FINAL COMMENT: _____

SIGNED _____ ANESTHETIST.

FIGURE 7 (*continued*)

else at the present time, it seems to me, is a quick-acting gaseous agent which will produce reasonable extreme relaxation of the abdominal muscles with reasonably rapid recovery therefrom. This, it seems to me, cyclopropane shows some possible evidence of doing."

Professor Henderson, in answer to this letter, wrote (Fig. 8) pointing out that Dr. Waters should estimate the cyclopropane content of gaseous mixtures by dissolving it in sulphuric acid and should not assume that all the gas remaining after the removal of oxygen and carbon dioxide was cyclopropane (Fig. 5). I recall that Dr. Waters reported later that the analyses made by the Toronto method showed that the anaesthetic concentrations of cyclopropane were about half that reported in his first three cases.

The friendship, interest, and co-operation of two doctors outside of Toronto were largely responsible for the employment of cyclopropane clinically. Dr. Ralph M. Waters and Dr. Harold R. Griffith were present in Montreal at the meeting of the Canadian Medical Association in June, 1929, when Professor Henderson announced our discovery of cyclopropane as a general anaesthetic. They were much interested in the gas and followed our progress with it. Dr. Griffith became interested in Dr. Waters' success in the Wisconsin General Hospital and a paper presented by Stiles, Neff, Rovenstine, and Waters at the 12th Annual Congress of Anaesthetists in Chicago, October, 1933 (12), convinced him of its clinical value and led him to begin using it as a general anaesthetic in the Homeopathic Hospital of Montreal in 1933. He thus became the first anaesthetist in Canada to employ cyclopropane.

Pharmacology of Cyclopropane

Cyclopropane (trimethylene) was prepared in 1882 by Von Freund. It was made from trimethylene bromide plus zinc dust. Later it was made from 1-3-dichlorpropane plus zinc. This latter method is known as the Haas method. The anaesthetic potency of cyclopropane was determined in 1928–9 by Lucas and Henderson (10). Its molecular weight is 42.05; its specific gravity 1.46 (air—1). It liquefies at 5 atmospheres pressure at room temperature; the boiling point is −34.4° C. It is rapidly absorbed by sulphuric acid, a property which makes it easy to analyse when in combination with other gases. It is stable when stored in liquid form in steel alloy tanks at room temperature. The impurities occurring in it may be propylene, propane, allene, organic halides, and cyclohexane. Some of these are formed during its manufacture. The solubility in oil as compared to water is 34.4; oil as compared to blood 15.3. The flash point of this material is below 0° C. The minimum ignition temperature is 927° F. in air and 849° F. in oxygen.

It is a colourless gas, non-irritating to the respiratory tract. It has a sweetish odour and taste. It is inflammable and, according to my notes, forms an explosive mixture in anaesthetic concentrations (Fig. 9); in air, mixtures of 2.4 to 10.3 per cent and oxygen 2.5 to 60 per cent are explosive. It is not altered in the body. The major portion is eliminated from the body in 10 min., but for complete desaturation of the tissues a number of hours are required. No histological changes occur in any of the organs.

September 8, 1930.

Dr.R.M.Waters,
Dept. of Anesthesia,
State of Wisconsin General Hospital,
Madison, Wis.

Dear Dr.Waters:

I am sorry to have delayed in acknowledging your letter of August 20th, which came while I was away on holidays, and not easily reached.

Your experience is extremely interesting and valuable to us. Our experiments with the human anesthetics have not proceded very far, owing to various delays and holidays. Consequently, we cannot give you very intellignet criticism on your findings. We are, however, extremely doubtful if such a high percentages are required.

As far as we can judge from your letter and charts, you estimate the amount of cyclopropane by analyzing for oxygen and carbondoxide and considering the residue of cyclopropane. We are quite sure that this will not give you accurate results. Any gas unabsorbable by pyrogallol will then be aounted cyclopropane. Cyclopropane can be absorbed by strong sulphuric acid, and all our calculations of anesthetic concentration have been based on such an analysis. We find in one sample of cyclopropane a considerable amount of unabsorbable gas, either a saturated hydrocarbon which is apt to be present in small amounts, or nitrogen.

We will let you know when we have tried some more experiments.

Yours sincerely,

FIGURE 8. Facsimile of a letter from Professor Henderson to Dr. Waters.

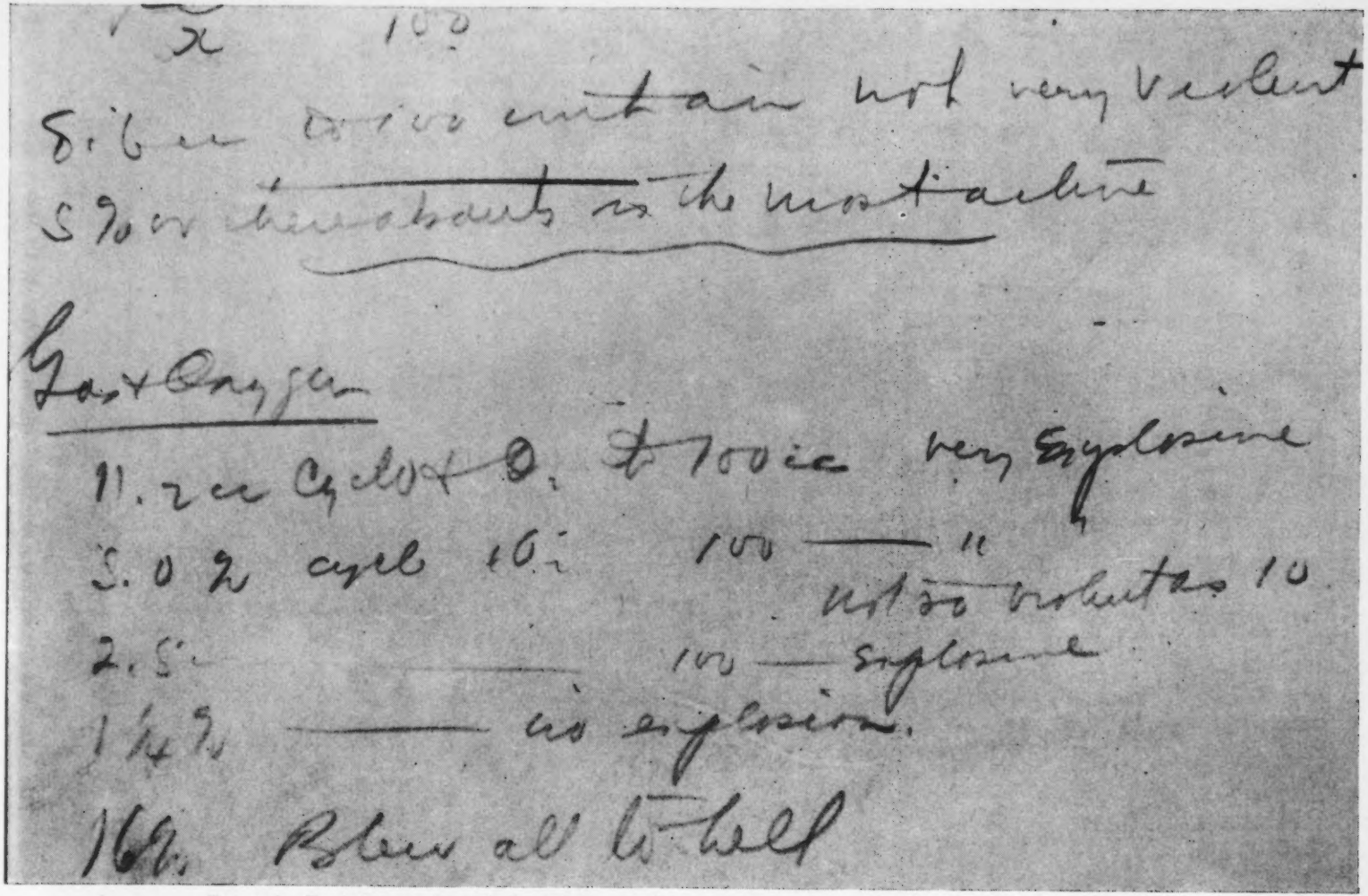


FIGURE 9. Facsimile from the author's notebook recording experiments on the explosability of cyclopropane in oxygen.

On inhalation laryngospasm may develop during induction or during very light anaesthesia, possibly owing to the parasympathomimetic action of the gas; atropine and scopolamine medication ordinarily inhibit this effect. Laryngospasm may occur if high concentrations are inhaled.

During cyclopropane anaesthesia, dreams do not occur as they do when nitrous oxide or ethylene is administered.

Analgesia occurs when concentrations of 3 per cent to 5 per cent of the gas are inhaled. Plane II requires from 11 to 14 per cent; plane III, 14 to 23 per cent; plane IV, 23 to 40 per cent. At this high concentration respiration may fail. The gas is administered in a closed circuit and is not altered by alkaline absorbants or carbon dioxide. The kidneys, liver, spleen, and uterus are little affected during anaesthesia. The activity of the intestine is depressed in deep anaesthesia, but recovery is rapid when the gas is withdrawn. Blood-clotting time is unchanged although oozing and capillary bleeding are encountered owing to vasodilation and to some elevation of the blood pressure. Metabolic processes and blood chemical patterns are not disturbed significantly.

Relaxation of skeletal muscle is adequate for many surgical operations. The gas may be administered with muscle relaxants such as curare to gain greater relaxation.

The most serious disadvantage of cyclopropane lies in the fact that the irritability of the automatic tissue of the heart is increased, causing arrythmias from the displaced pacemaker. Vagus escape, atrioventricular block, ventricular tachycardia, and ventricular fibrillation may occur spontaneously. The mechanism by which this anaesthetic adversely influences cardiac automaticity is not completely understood, although much research has been directed to the solution of the problem and a voluminous literature exists. There is some evidence that sympathetic reflexes arising in abdominal receptors play a role in the production of these cardiac disorders.

It has been known for a long time that epinephrine and some related amines enhance the production of the arrythmias, but the mechanisms involved are subject to much debate. In the opinion of some workers both the rise in blood pressure and the direct effect of epinephrine must be considered.

Epinephrine is lost from the adrenal gland during cyclopropane anaesthesia but less so than with ether. Ether, however, protects the heart from cyclopropane arrythmias when it is administered with the gas.

The proper choice of drugs for premedication may play an important role in the incidence of cyclopropane arrhythmias. There is some support for the belief that they arise more frequently with morphine than with barbiturates. The content of potassium in the myocardium may also play some role in the occurrence of arrhythmias in cyclopropane anaesthesia. It has been shown that an increase of the potassium in the myocardium follows the injection of epinephrine. Anoxia, an excessive rise in carbon dioxide, alkalosis, and a rise in blood sugar may also contribute to such irregularities.

Atalectasis, partial or massive, may occur, it is claimed, if the anaesthetist does not watch his patient carefully to be sure of adequate respiration and to see that some inert gas such as nitrogen or helium is left in the inspired air after cessation

Scanned from the author's notebook recording experiments on the explosability of cyclopropane in oxygen.

of the operation. Cyclopropane and oxygen are rapidly absorbed and unless some less soluble gas is in the lungs, areas may collapse.

Following long operations, postoperative hypotension may occur (cyclopropane shock). This condition appears to be associated with a severe respiratory acidosis. It is believed that the proper prophylaxis to prevent this syndrome may be achieved by maintenance of a normal alveolar carbon dioxide tension.

Experimentally on dogs, employing the cyclopropane-epinephrine test, investigators have reported that procaine amide, procaine, meperidine, quinidine, atropine (large doses), ergotamine, dibenamine, and tolazoline afford partial or complete protection against cardiac arrhythmias.

I have taken considerable time to discuss the early history of the research on anaesthesia in the Department of Pharmacology and to show how the pioneer investigations of the late Dr. Velyien E. Henderson and the late Dr. W. Easson Brown led to our discovery of cyclopropane. It was my good fortune to be associated with them in this work.

It is fortunate, also, that my notes on the preparation and first use of the gas experimentally on animals have been preserved, together with some of the apparatus used in the experimental investigations, and that I found Dr. Waters' letter to Professor Henderson, along with copies of the hospital records of Dr. Waters' three patients, and the copy of Dr. Henderson's reply.

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A STUDY OF CHLOROFORM ANAESTHESIA IN A PRECISION SYSTEM: I. THE EFFECT ON ANION–CATION BALANCE IN MAN[1]

ALLEN B. DOBKIN, M.D., HUGH J. JOHNSTON, M.D., and LESLIE C. SKINNER, M.B.

MUCH HAS BEEN WRITTEN during the last century about the clinical use of chloroform. Its potent effects on respiration, circulation, and hepatic activity have been stressed repeatedly. Re-evaluations have been described during the past decade (1, 2, 3, 4). The most important requirement which is still not generally available is a precision vaporizer that would facilitate gradual and accurate alterations in the concentration of inhaled vapour. An absolute requirement to avoid serious cardiovascular and metabolic derangements is the assurance that no hypoxia or hypercarbia develops during administration of chloroform. This report deals with the effect of chloroform anaesthesia on anion–cation balance when administered in a precision system.

MATERIALS AND METHODS

Data were collected from 50 patients. Each was premedicated orally the evening before an elective operation with 200 mg. meprobamate and 25 mg promazine (Equazine ®). About one hour before induction of anaesthesia, 5 mg. of perphenazine was given intramuscularly with 0.4 mg. scopolamine. Patients over 60 years of age received 0.4 to 0.6 mg. atropine instead of scopolamine. Anaesthesia was induced with a sleep dose of 2.5 per cent thiopental intravenously, following a dose of dimethyl d'tubocurarine or gallamine that was considered sufficient to facilitate endotracheal intubation. In each case, intubation was preceded by artificial respiration with 100 per cent oxygen for about one minute. Anaesthesia was then maintained in a non-rebreathing system with nitrous oxide, oxygen (2:1) and chloroform—which was delivered through a "Chlorotec" calibrated temperature-compensating vaporizer (Fig. 1). A supplementary dose of atropine was administered after induction of anaesthesia, and this was repeated during long operative procedures, and whenever a marked slowing of the pulse rate was observed. Small doses of the muscle relaxant initially selected were given during maintenance of anaesthesia if necessary.

For each patient, pulmonary ventilation was regulated mechanically using a Takaoka respirator. This instrument cycles automatically with an inspiratory phase slightly shorter than the expiratory phase. Inspiratory pressures vary approximately between 12 and 20 mm. Hg, depending mainly on rate of gas inflow used. A fixed negative pressure of 3 to 4 mm. Hg occurs during expiration. Rate of cycling was always set at 18 per minute. Minute volume was monitored with either an Ohio minute volume meter or a Wright respirometer, and was

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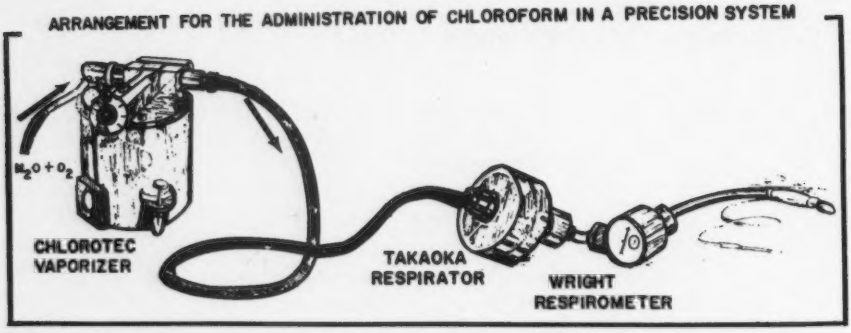


FIGURE 1. Arrangement for the administration of chloroform in a precision system.

adjusted by altering the gas inflow until the patient's tidal volume approximated the volume indicated as ideal by the Radford nomogram, and corrected according to factors relating the patient's age and body build, the posture adopted for the operation, and the presence of emphysema or cardiac incompetence (5).

A stable level of anaesthesia was usually achieved within a few minutes after induction, using 0.5 to 1.0 per cent chloroform. During the operation, 5 per cent dextrose in water was administered intravenously unless a whole blood transfusion was necessary. No electrolyte solutions were administered during any of these operations. Hypothermia and hypotension were not induced intentionally in any of these patients.

Anion–cation changes were determined from blood samples which were drawn anaerobically, using the brachial artery in most cases. In a few cases arterialized blood was taken from the median cubital vein (6). The blood samples were drawn shortly before induction, at 30 to 45 min. intervals during maintenance of anaesthesia, immediately after extubation at the end of the operation, and again 30 min. later in the recovery room. They were analysed immediately for pH, total CO_2, haematocrit value, and in most cases, for oxygen saturation, employing standard laboratory techniques that were described in previous reports (7, 8, 9). Plasma CO_2, pCO_2, plasma bicarbonate, and fixed acid changes were calculated from the above data. The pH and plasma bicarbonate values were plotted on a graph as recommended by Davenport and Weisberg (10, 11).

RESULTS

The pertinent data from the blood analyses appear in Table I, which is divided into four parts on the basis of the patient's age. Figure 2 shows the mean shifts in pH, pCO_2, and plasma bicarbonate in the four age groups. Statistical analyses of the data from each group showed that a change occurred from the samples drawn before induction and those drawn 30 to 45 min. later. This change was in the direction of a moderate respiratory alkalosis. No significant metabolic change was evident. During long maintenance there was a slow return to the preoperative state. Blood samples drawn postoperatively showed only a slight reduction of fixed base.

TABLE I

Data from Serial Blood Analyses to Show Effect of Chloroform on Anion–Cation Balance

						Before anaesthesia				Steady anaesthesia				During maintenance				End of anaesthesia				30 min. after anaesthesia			
Age	Build	Phys. Status	Posture	Op. Site	Anaesth. time (min.)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)
18	O	2	S	↑A	90	7.46	88	28	19	7.60	100	21	20.2	7.54	100	23	19.8	7.51	91	25	19.5	7.51	92	27	20.7
28	O	2	P	Spine	225	7.28	68	62	25	7.39		42	23.3	7.38		43	22.8 (4)*	7.26		50	20.1	7.25	77	51	19.9
33	M	1	S	↑A	170	7.42		20	13.5	7.45		19	13.5	7.47		20	12 (3)	7.44		27	18	7.40		30	18
34	M	1	S	↑A	130	7.23		56	20.5	7.22		51	19	7.22		47	17.9	7.21	..	48	18.1	7.22		45	17.3
37	M	1	S	↑A	150	7.33	90	46	22	7.45	89	36	23	7.37	90	39	20.2 (2)	7.36	87	39	20.2	7.30	82	48	22
37	M	1	S	↑A	145	7.38	96	40	21.7	7.38	100	38	21	7.33	100	44	21.3 (2)	7.28	100	43	19.1	7.29	92	38	17
39	O	2	S	↑A	280	7.29	95	51	22	7.41	97	37	21.9	7.38	98	38	20.9 (4)	7.37	97	32	17.3	7.31	96	43	20.3
41	M	1	T	↓A	165	7.32	79	47	22.4	7.38	90	37	20.3	7.39	91	37	20.8 (2)	7.38	91	34	18.9	7.30	94	42	20
43	M	1	S	↑A	100	7.38	93	34	19	7.52	100	22	17.9	7.52	99	22	17.8	7.44	99	27	18	7.35	99	36	18.9
44	L	2	S	↑A	215	7.37	95	38	20.3	7.40	83	32	18.5	7.41	77	27	17.0 (2)	7.38	92	35	19.2	7.33	94	37	18.3
45	M	1	P	Spine	320	7.47	93	31	20.2	7.49	78	25	18.4	7.48	80	25	18.1 (8)	7.44		32	20.1	7.47	100	31	21.2
45	M	1	S	↑A	145	7.38	86	42	23	7.41	91	37	21.6	7.50	100	30	22	7.46	96	31	20.9	7.37	97	44	23
45	O	2	S	↑A	180	7.39	94	33	18.8	7.41	90	30	18.2	7.40	95	32	19 (3)	7.21	88	50	18.4	7.19	96	49	17.2
48	L	3	S	↑A	135	7.38	94	41	22.7	7.57	100	27	23	7.48	100	33	22.1	7.32	100	50	23	7.37	100	41	17.9
50	O	2	S	Neck	110	7.46	94	36	23.5	7.48	97	29	20.9	7.48	97	29	20.2	7.48	91	29	20.3	7.47	84	31	17.2
Mean 39					171	7.37	90	40	21.0	7.44	93	32	20.0	7.42	93	33	19.5	7.37	94	37	19.4	7.34	92	40	19.3
S.D.						.07	8	11	2.7	.09	7	9	2.6	.08	8	9	2.7	.09	5	9	1.4	.09	7	7	1.9
S.E.						.02	2	3	0.7	.02	2	2	0.7	.02	3	2	0.7	.02	1	2	0.4	.02	2	2	0.5

L = lean
M = medium
O = obese

↑A = Upper Abdomen
↓A = Lower Abdomen
C = Intrathoracic
AP = Abdominoperineal

*Figures in parentheses indicate averaged data from the number of blood samples noted.

TABLE I (*continued*)

							Before anaesthesia				Steady anaesthesia				During maintenance				End of anaesthesia				30 min. after anaesthesia			
	Age	Build	Phys. Status	Posture	Op. Site	Anaesth. time (min.)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)
	53	O	3	S	†A	65	7.33	96	42	21.2	7.47	96	30	19.8	7.49	96	28	20	7.33	80	41	20	7.33	81	41	20.2
	54	O	2	S	†A	155	7.39	88	46	24.9	7.45	94	38	24	7.45	93	39	24.8 (3)*	7.46	90	36	22.5	7.38	86	39	21.8
	54	O	2	S	†A	290	7.46		25	14.3	7.40		27	17	7.36		31	17.3 (3)	7.31		31	15.5	7.34		28	14.9
	54	M	3	S	†A	165	7.24		50	19.9	7.24		47	18.7	7.32		37	18	7.31		41	19	7.17		56	19
	54	O	2	S	†A	80	7.31	94	45	19.7	7.40	95	38	22	7.40	95	38	22	7.35	85	43	22.5	7.31	67	47	21
	55	M	3	S	†A	135	7.52	79	25	20	7.56	94	20	17.8	7.60	95	19	18.9	7.50	99	24	18.5	7.43	100	28	18.2
	55	O	2	S	†A	250	7.36	92	43	23.9	7.45	97	34	20.3	7.38	96	41	21.8 (3)	7.32	100	47	22.8	7.38	95	39	22
	56	L	2	S	†A	230	7.37		32	15.9	7.44		29	19	7.44		28	18.7 (5)	7.39		28	16.5	7.36		30	16.8
	57	O	3	S	†A	250	7.31	86	49	20.9	7.50	93	30	22	7.47	95	30	20.2 (3)	7.27	91	55	23	7.20	92	62	22
	57	O	3	S	†A	150	7.44	91	35	21.2	7.40	94	42	23.5	7.37	97	47	24.4 (2)	7.37	96	45	23.4	7.36	87	43	22.8
	57	M	3	L	C	255	7.43	78	34	20.5	7.46	74	32	21	7.36	87	39	20.8 (3)	7.28	89	40	20	7.25	60	47	19.7
	59	O	2	S	†A	185	7.29	92	47	19.8	7.43	91	34	20.5	7.37	92	37	20 (4)	7.18	100	53	17.9	7.34	89	39	19.8
	59	O	2	S	†A	90	7.41	83	38	22.5	7.50	86	30	22	7.46	100	34	21	7.42	99	38	23	7.37	91	42	22.9
	59	O	2	L	C	150	7.42	94	34	20.9	7.43	90	36	22.4	7.36	95	38	20.1	7.24	92	56	22	7.32	91	39	19
Mean	56					175	7.38	88	39	20.4	7.44	91	33	20.7	7.42	95	35	20.6	7.34	93	42	20.5	7.32	85	41	20.0
S.D.							.08	6	8	2.7	.07	6	7	2.1	.07	3	7	2.2	.09	7	10	2.6	.07	12	10	2.3
S.E.							.02	2	2	0.7	.02	2	2	.6	.02	.3	2	0.6	.02	2	3	0.7	.02	4	3	0.6

TABLE I (*continued*)

	Age	Build	Phys. Status	Posture	Op. Site	Anaesth. time (min.)	Before anaesthesia				Steady anaesthesia				During maintenance				End of anaesthesia				30 min. after anaesthesia			
							pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)
	60	M	2	S	↑A	310	7.35	94	42	20.8	7.48	96	28	19.8	7.30	90	45	19.9 (4)*	7.35	92	38	19.8	7.30	94	40	18.9
	60	M	1	S	↑A	120	7.43	92	36	22.6	7.49	94	27	20	7.39	100	33	18.9	7.38	100	38	20.9	7.36	82	39	20.9
	61	L	3	L	C	290	7.39	86	38	20.5	7.40	80	41	23.8	7.31	90	47	20.8 (3)	7.31	88	45	20.1	7.29	88	47	21.2
	63	O	3	S	↑A	225	7.41	88	37	22	7.35	95	40	20	7.38	97	43	20.6 (3)	7.23	90	54	20	7.35	85	37	19.8
	65	O	3	S	↑A	105	7.38	82	45	23	7.36	90	49	24.9	7.36	92	49	24.9	7.31	94	55	25	7.30	93	54	24.8
	66	O	2	T	↓A	230	7.32	93	36	17.9	7.32	91	35	17.1	7.36	92	32	17.4 (2)	7.32	96	37	18	7.16	100	58	19
	67	O	2	T	↓A	145	7.35	90	41	20	7.49	91	31	20.4	7.54	93	25	21	7.60	93	20	19.7	7.44	100	31	20
	67	L	1	S	↑A	190	7.30		47	20.5	7.31		42	19.7	7.32		42	19.9 (2)	7.30		43	19.8	7.32		43	20.9
	68	M	3	S	↑A	90	7.33	90	42	20	7.34	88	41	20.9	7.37	97	37	20	7.25	94	51	19.9	7.35	95	36	18.9
	68	M	2	S	↑A	100	7.36	95	43	22.7	7.56	98	26	22.5	7.56	98	26	21.9	7.37	100	43	22	7.41	100	37	22
Mean	65					180	7.36	89	41	21.0	7.41	91	36	20.9	7.38	94	38	20.5	7.34	94	42	20.5	7.33	93	42	20.6
S.D.							.04	5	4	1.6	.09	5	8	2.3	.09	4	9	1.9	.10	4	10	1.9	.08	7	8	2
S.E.							.01	2	1	0.5	.03	2	2	0.7	.03	1.2	3	0.6	.03	1.4	3	0.6	.02	2	3	0.6

TABLE I (*continued*)

	Age	Build	Phys. Status	Posture	Op. Site	Anaesth. time (min.)	Before anaesthesia				Steady anaesthesia				During maintenance				End of anaesthesia				30 min. after anaesthesia			
							pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)	pH	O_2 sat. (%)	pCO_2 (mm. Hg)	HCO_3^- (mM/L)
	71	L	3	S	↑A	90	7.32		45	21.6	7.32		48	23	7.32		48	23	7.32		49	23	7.30		49	22.9
	71	L	3	S	↑A	170	7.38	98	47	25	7.23	98	69	26	7.51	99	35	26 (2)*	7.50	100	35	25.5	7.38	100	47	25.5
	71	L	2	S	↑A	125	7.36	96	43	22.5	7.45	97	31	20.9	7.45	99	31	21	7.34	99	43	21.1	7.32	99	40	19.8
	71	M	3	TL	↓AP	250	7.35		35	18	7.39		27	15.5	7.29		29	13.9 (3)	7.15		48	16	7.06		58	15.5
	72	M	3	S	↑A	105	7.40	95	38	22	7.59	98	24	22.6	7.56	100	25	21.8	7.46	100	29	19.9	7.34	96	41	21.2
	73	M	2	TL	↓AP	170	7.37	86	42	23	7.43	91	34	21.4	7.49	91	30	21.9 (2)	7.42	97	34	20.8	7.36	92	43	23
	73	O	3	S	↑A	270	7.52	92	28	22	7.56	100	23	20	7.39	100	30	17.6 (3)	7.28	100	42	18.9	7.25	92	41	17.4
	73	O	4	S	↑A	170	7.28	88	43	18.7	7.41	94	30	18.3	7.46	97	26	18 (3)	7.47	96	25	18	7.28	89	41	18.7
	76	M	1	S	↓A	135	7.31		43	20.6	7.39		35	19.9	7.38		30	17 (2)	7.31		39	18.9	7.32		38	18.6
	79	L	3	S	↑A	120	7.26	81	42	18	7.34	98	36	18.7	7.34	100	36	18.9	7.22	100	44	16.9	7.24	100	45	18.7
	81	M	3	S	↓A	80	7.34		28	15	7.47		22	15.9	7.42		22	14	7.47		20	14.8	7.38		31	17.9
Mean	74					153	7.35	91	39	20.4	7.42	97	35	20.2	7.42	98	31	19.4	7.36	99	37	19.4	7.29	95	43	19.9
S.D.							.07	6	6	2.9	0.10	3	14	3.1	.08	3	7	3.7	0.11	2	9	3.1	.09	4	7	2.7
S.E.							.02	2	2	0.9	.03	1	4	0.9	.03	1	2	1.1	.04	1	3	0.9	.03	2	2	0.8

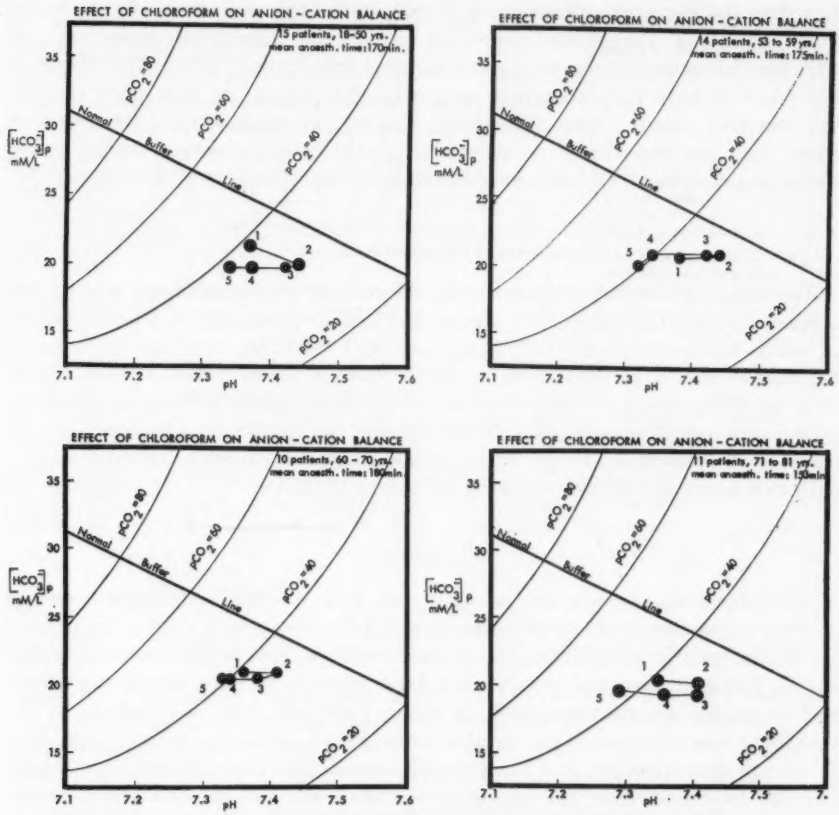


FIGURE 2. Represents the mean plasma bicarbonate, pH, and pCO_2 in the arterial blood in four groups of patients during chloroform–nitrous oxide anaesthesia. The numbered points indicate: (1) before induction of anaesthesia; (2) after a stable surgical plane of anaesthesia was in progress for 30 to 45 min.; (3) mean values from blood data obtained at 30 to 45 min. intervals during maintenance; (4) immediately after extubation and breathing spontaneously; (5) 30 min. after anaesthesia.

In most of the patients, there was an improvement in oxygen saturation after induction of anaesthesia, which was maintained until the end of the operation. In some patients this fell sharply in the immediate postoperative period necessitating the administration of oxygen in the recovery room. This was done routinely for the elderly and poor risk patients, to avoid hypoxia.

Smooth anaesthesia was maintained without difficulty, chloroform being employed in a concentration which exceeded 1 per cent briefly in only two instances. The remaining patients required no more than 0.5 to 1 per cent chloroform even during the strong stimulation that occurred during upper abdominal operations. During many operations when stimulation was minimal,

less than 0.5 per cent chloroform was sufficient. After peritoneal closure in the long operations, the chloroform could usually be turned off completely, as sufficient anaesthesia persisted until surgical stimulation terminated. Most of the patients were fully conscious soon after extubation, or after they reached the recovery room. Three anaesthetic charts and corresponding protocols of blood data are reproduced to show the typical course observed during intrathoracic and upper and lower abdominal operations (Figs. 3, 4, 5).

Discussion

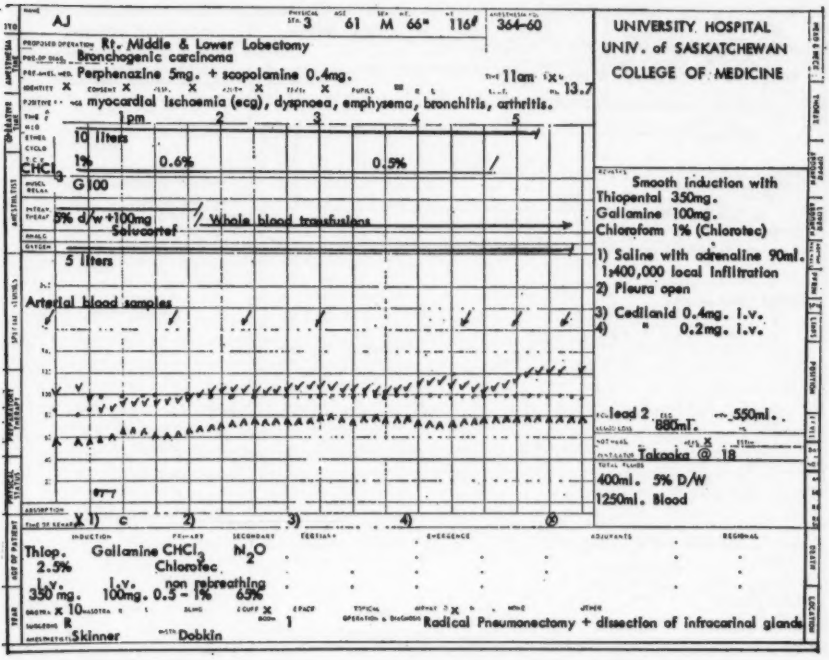
The minor alterations accompanying chloroform–N_2O anaesthesia which were observed during this study were almost identical to those seen in a similar study in which trichlorethylene–N_2O, halothane–N_2O, and the azeotropic mixture of halothane–ether were used (7, 8, 9). On the basis of anion–cation balance, therefore, no difference is evident between these three agents as long as adequate pulmonary ventilation is assured throughout the period of administration of chloroform anaesthesia. However, smooth anaesthesia was very easy to maintain with this agent as has been reported by others (2, 3, 4).

Summary

Chloroform anaesthesia was administered with nitrous oxide–oxygen during elective major operations to 50 patients, employing a specially calibrated vaporizer (Chlorotec) in a non-rebreathing system. Artificial respiration was provided with a Takaoka ventilator which has a fixed negative pressure during expiration and a variable minute volume which can be regulated. The tidal volume of the ventilator was adjusted to the requirements of each individual patient according to his age, size, posture, and cardiorespiratory status. Data derived from blood samples indicated that chloroform anaesthesia did not disturb anion–cation balance when administered in this way, and the administration of chloroform had no depressant effect on the oxygen saturation of the blood. The maintenance of a stable level of surgical anaesthesia was accomplished in this system with less than 1 per cent chloroform. On the basis of these observations, little difference was evident between chloroform and other potent anaesthetic agents which have been studied in a similar manner.

Résumé

A 50 malades au cours d'opération majeures, nous avons donné une anesthésie au chloroforme avec protoxide et oxygène en employant un vaporisateur (Chlorotec) calibré spécialement pour le chloroforme et un circuit sans réinspiration. Nous avons entretenu une respiration artificielle à l'aide du ventilateur de Takaoka; ce ventilateur applique une pression négative uniforme à l'expiration et peut donner un volume minute variable que l'on peut déterminer. L'air courant du ventilateur a été fixé selon les exigences des malades, exigences variant selon leur âge, leur taille, leur position et leur état cardiorespiratoire. D'après les résultats des ana-

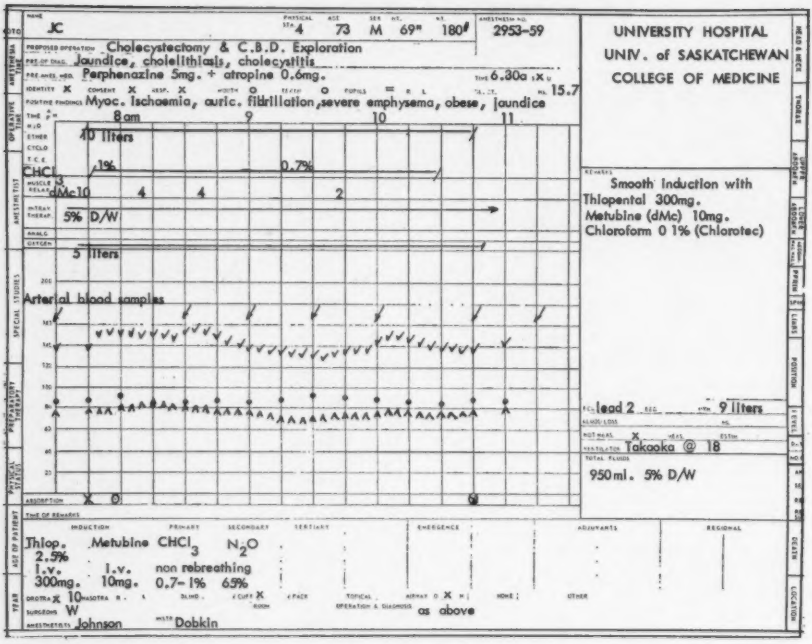


Patient AJ Hosp.# 89549C Age 61 Sex M Ht. 66" Wt. 116 B.S.A.1.60 Physical State 3 Build Lean
Anaesth.# 364-60 Premed.: Perphenazine 5mg. + Scop.: 0.4mg. Anaesth.: Thiop. 350 + G 100 + N_2O – Chloroform
Pulm. Vent.: Method – TAKAOKA Amplitude +13, –4 Phases 2
Blood Pressures: Preop.: 106/60 During Anaesth.: Steady – 104/78 Postop.: Steady – 126/84

Ventilation Data	Control /	General Anaesthesia				/ Postop.
Time	12.00	1.30	2.15	3.00	4.30	5.00	5.30
Tidal Volume ml.	S.R.	550	550	550	550	A.R.	S.R.
Rate / min.	15	18	18	18	18	20	24
Minute Volume liters		9.9	9.9	9.9	9.9		
Arterial Blood DATA							
Hgb.	13.7						14.0
Hct.	39	39	41	43	43	42	41
pH	7.39	7.40	7.38	7.27	7.29	7.31	7.29
Total CO_2 content mM/L	23.3	26.2	23.0	25.5	24.5	23.0	23.0
Plasma HCO_3^- mM/L	20.5	23.8	23.2	22.6	21.4	20.1	21.2
pCO_2 mm.Hg.	38	41	38	54	50	45	47
% O_2 saturation.	80	86	92	92	88	90	88

Summary & Remarks: Rt. radical pneumonectomy. Lateral flexed position. Anaesthesia was maintained for 290 minutes with Chloroform (0.5 – 1%) in a Chlorotec vaporizer and Nitrous oxide – Oxygen (2:1) in a nonrebreathing system. Pulmonary ventilation was controlled with a TAKAOKA respirator and monitored with the Wright respirometer. ECG lead 2 was monitored throughout – no arrhythmias were observed. Slight respiratory acidosis developed after the right bronchus was opened and the lung was removed. Otherwise the patient's course during anaesthesia was uneventful and his postoperative course was free from anaesthetic and surgical complications in spite of myocardial ischaemia, severe bronchitis and emphysema.

FIGURE 3. Anaesthetic chart and blood data protocol. Observe the relatively stable vital signs during 4 hrs. of thoracic surgery. Muscle relaxant was required only for intubation. 0.8 per cent chloroform was administered until chest closure was started.

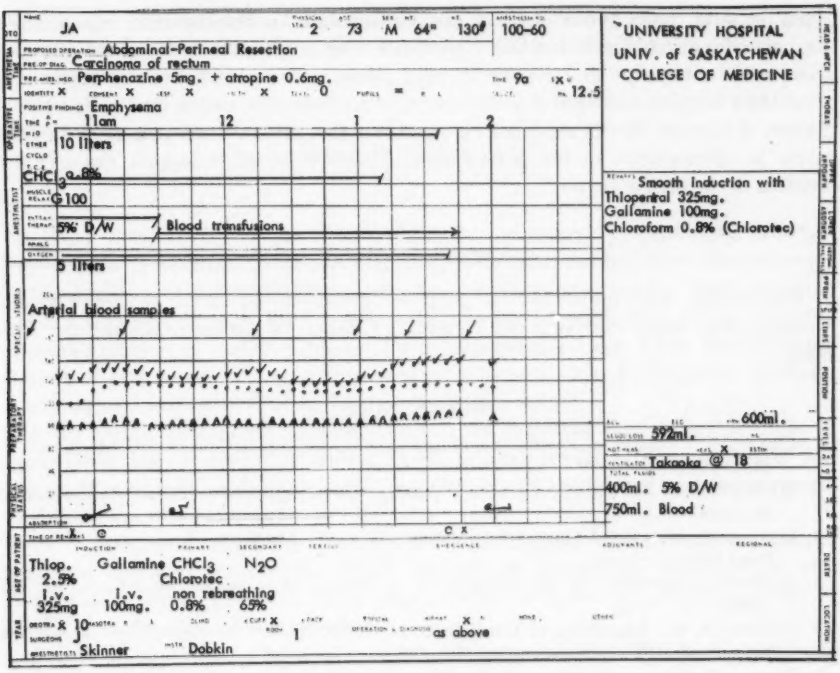


Patient JC Hosp.# 48056 Age 73 Sex M Ht. 69" Wt. 180# B.S.A. 1.96 Physical State 4 Build Obese
Anaesth.# 2953-59 Premed.: Perphenazine 5mg. + Scop. 0.4mg. Anaesth.: Thiop. 300 + dMc 22 + N_2O - Chloroform
Pulm. Vent.: Method-TAKAOKA Amplitude +15, -4 Phases 2
Blood Pressure: Preop.: 138/78 During Anaesth.: Steady - 144/78 Postop.: Steady - 130/90

Ventilation Data	Control	General Anaesthesia					Postop.
Time	7.30	8.30	9.00	9.30	10.00	10.45	11.15
Tidal Volume ml.	S.R.	500	500	500	500	±S.R.	S.R.
Rate/min.	16	18	18	18	18	22	20
Minute Volume liters		9	9	9	9		
Arterial Blood Data							
Hgb.	15.7						15.4
Hct.	47						
pH	7.28	7.41	7.46	7.47	7.45	7.47	7.28
Total CO_2 content mM/L	21.2	19.5	18.0	18.0	19.2	18.5	20.0
Plasma HCO_3^- mM/L	18.7	18.3	18.0	18.0	18.0	18.0	18.7
pCO_2 mm.Hg.	43	30	26	25	27	25	41
% O_2 saturation	88	94	97	97	97	96	89

Summary & Remarks: Cholecystectomy & C.B.D. Exploration. Supine horizontal position. Anaesthesia was maintained for 170 minutes with Chloroform (0.7 - 1%) in a Chlorotec vaporizer and Nitrous oxide - Oxygen (2:1) in a nonrebreathing system. Pulmonary ventilation was controlled with a TAKAOKA respirator and monitored with the OHIO ventilation meter. ECG lead 2 was monitored throughout (auricular fibrillation). Even though this patient was a poor risk (myocardial ischaemia, severe emphysema, jaundice, obese) he had a smooth anaesthetic and an uneventful postoperative course.

FIGURE 4. Anaesthetic chart and blood data protocol. Observe the stable vital signs throughout the anaesthetic. This patient required more muscle relaxant than was usual.



Patient JA Hosp.# 52411 Age 73 Sex M Ht. 64" Wt. 130# B.S.A. 1.62 Physical State 2 Build Medium

Anaesth.# 100–60 Premed.: Perphenazine 5mg. + Atr. 0.6mg. Anaesth.: Thiop. 325 + G 100 + N_2O – Chloroform

Pulm. Vent.: Method– TAKAOKA Amplitude +15, –4 Phases 2

Blood Pressure: Preop.: 120/84 During Anaesth.: 124/86 (Steady) Postop.: 138/90 (Steady)

Ventilation Data	Control	General Anaesthesia				Postop.
Time	10.15	11.15	12.15	1.00	1.20	1.50
Tidal Volume ml.	S.R.	600	600	600	S.R.	S.R.
Rate/min.	15	18	18	18	16	22
Minute Volume liters		10.8	10.8	10.8		
Arterial Blood Data						
Hgb.	12.5					11.7
Hct.	38	40	42	40	40	41
pH	7.37	7.43	7.49	7.49	7.42	7.36
Total CO_2 content mM/L	24.5	22.5	24.0	23.2	22.5	24.5
Plasma HCO_3^- mM/L	23.2	21.4	21.9	21.9	20.8	23.0
pCO_2 mm.Hg.	42	34	31	30	34	43
% O_2 saturation	86	91	88	94	97	92

Summary & Remarks: Resection Large Bowel (Ca. Recto-sigmoid). Lithotomy – head low position. Anaesthesia was maintained for 170 minutes with Chloroform (0.5 – 1%) in a Chlorotec vaporizer and Nitrous oxide – Oxygen (2:1) in a nonrebreathing system. Ventilation was controlled with a TAKAOKA respirator and monitored with a Wright respirometer. Anaesthetic and postoperative course were uneventful.

FIGURE 5. Anaesthetic chart and blood data protocol. Observe very smooth anaesthetic course during an abdominal perineal operation.

lyses de sang, nous avons observé que l'anesthésie au chloroforme, administrée de cette façon, n'a pas modifié l'équilibre électrolytique et, de plus, n'a pas diminué la saturation en oxygène du sang. Nous avons réussi, avec ce système, à maintenir un plan constant d'anesthésie chirurgicale avec moins de 1% de chloroforme. A la suite de ces expériences, nous n'avons observé que peu de différence entre le chloroforme et les autres agents anesthésiques puissants qui ont été étudiés de la même façon.

Acknowledgment

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SOME ASPECTS OF ANAESTHESIA FOR HEAD AND NECK SURGERY

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IN HEAD AND NECK SURGERY, as well as in neurosurgery, prolonged tranquil anaesthesia is essential. Subdued respiratory function results from our attempts to maintain a stable anaesthetic free from reflex disturbances. Even with an airway established with the largest possible endotracheal tube, it may appear that the patient is underventilated for a considerable time. Does the resultant degree of carbon dioxide retention present a hazard, or is it tolerable, partially compensated and reversible with the anaesthetic state?

With regard to induced hypotension, can we assist the prevention of unnecessary blood loss by discreet lowering of the arterial pressure to a point that will maintain adequate perfusion of vital organs without the hazard of cellular anoxia and intravascular clotting?

In an attempt to integrate the anaesthetic techniques with the clinical results, we have reviewed the records of 125 patients presented for maxillo-facial and radical neck surgery over a three-year period. Included is a small number of laryngectomies and laryngo-fissures.

Figure 1 shows that a large proportion of these patients fell into the older age groups. You will note the incidence of either hypertension or arteriosclerotic cardiovascular disease.

TECHNIQUES OF ANAESTHESIA

These operations have all been performed under general anaesthesia and the non-rebreathing system has been used in the majority. Spontaneous respirations are maintained with minimal resistance by using one of the non-rebreathing valves (Ruben, Fink, Stephens-Slater) or a Bullough circuit. Sudden increases in pressure within the Magill circuit may obstruct the exhalation port on the Fink valve and this also occurred occasionally with the Ruben valve. Because of this hazard, a blow-off valve is inserted at the machine end of the Magill circuit. The advantage of these two types of valve, however, is that they permit the employment of controlled respirations when necessary. With this system the anaesthetic machine can be well isolated from the surgical field. With the Stephens-Slater valve, respirations cannot be controlled unless the exhalation valve is compressed by the anaesthetist's thumb.

The arrangement used in laryngectomies after preparation of the laryngeal stoma is as follows. A breathing tube fitted with Stephens-Slater valve is placed in position before the patient is draped. The Boyan tube is cold-sterilized,

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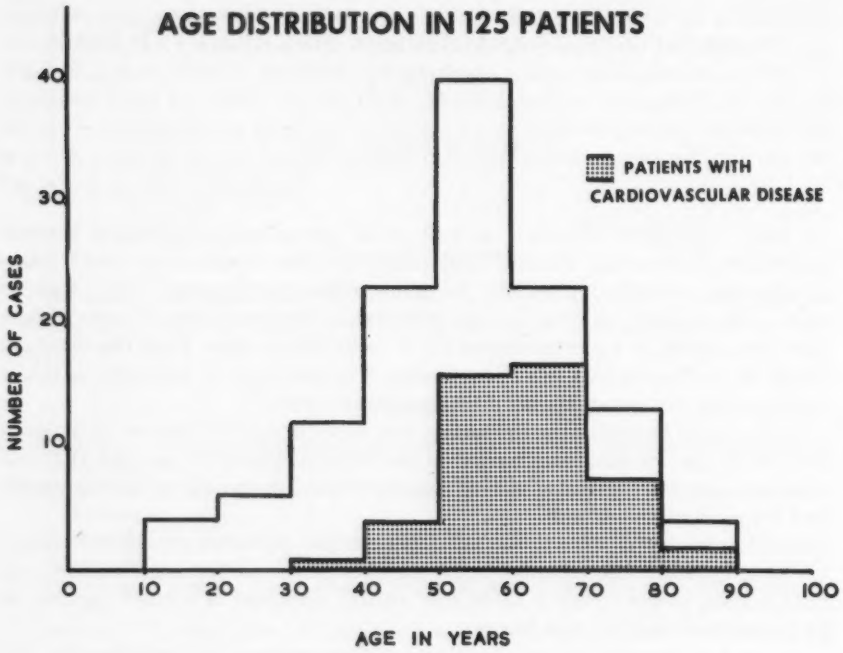

FIGURE 1

inserted into the stoma, and the cuff inflated. It is then connected to the valve under the drapes.

In a small number of cases regional nerve block was used in combination with supplementary general anaesthesia.

INDUCTION

Extra time taken to assure a tranquil induction pays handsome dividends in the form of diminished surgical haemorrhage. The acquisition of definite surgical anaesthesia is essential. It is fortified by the administration of a good topical anaesthetic nebulized through the vestibule of the larynx or injected through the cricothyroid membrane. A quiet nasal or oral intubation may then be performed. The absence of reflex disturbances avoids sudden increases in venous pressure. This in turn prevents the increased incisional bleeding that results from venous and capillary stasis. Omitting the use of a relaxant prior to intubation avoids interruption of spontaneous breathing.

ANAESTHETIC AGENTS

These patients were all maintained on a mixture of nitrous oxide and oxygen, and a non-rebreathing circuit was used in most instances.

During the preliminary stages of induction, a large number of these patients received a mixture designated as DLP which consists of meperidine (Demerol ®) 100 mg., chlorpromazine (Largactil ®) 50 mg., and promethazine (Phenergan ®) 50 mg. in a total volume of 20 cc. Some received varying amounts of this mixture plus thiopentone and meperidine. The incidence of respiratory depression and reflex disturbances in this group was high. This situation was improved by combination with volatile anaesthetic agents. With the addition of various volatile agents the anticipated effects were noted.

With trichlorethylene, there was a high incidence of tachypnoea, not reliably controlled by intravenous meperidine.

Ether was found to be quite satisfactory in cases where the use of electric cautery or coagulation was avoided. However, the incidence of post-anaesthetic nausea and retching was higher in this group.

Halothane began to be used late in 1956 and it has since been used in the majority of cases associated with a DLP induction. We note a smooth, easy induction and a decreased incidence of laryngospasm. Capillary oozing appears to be decreased. We have paid more attention to the patient's responses than to an accurate assessment of the concentration delivered. By varying the concentration within certain limits a reversible hypotensive effect is available and with care, cardiac disturbances rarely occur. The non-inflammability is an asset and a smooth undisturbed recovery common even after prolonged administrations. Our main concern has been the extremely high cost of this agent, particularly when used in a non-rebreathing circuit.

It was interesting to consider whether or not the cost could be decreased by reverting to the use of chloroform. With this in mind, chloroform was used in a small number of cases, intending to switch to ether to avoid prolonged administration. These patients were all attached to a cardiac monitor. Despite the fact that some of us had previous experience in the use of chloroform, we were surprised that the inductions were not as placid as with halothane. The incidence of cardiac arrhythmias was high, but may have been related to an unnecessarily high concentration. In one case chloroform was discontinued because of the occurrence of shifting pacemaker, extrasystoles, and hypotension. Halothane 0.5 per cent was substituted and no arrhythmias recurred over a period of several hours. Although a more detailed study is in order, our impression is that we cannot obtain comparable safe anaesthesia with chloroform.

This general method of anaesthesia for head and neck surgery produced satisfactory practical and clinical results. The inclusion of the ataractic cocktail naturally resulted in a prolonged recovery time, but this has been quite acceptable in patients undergoing such drastic and often disfiguring surgery. A common observation was that the patient's respiratory function appeared to be subnormal. There are two schools of thought concerning breathing during operation. One group believes any form of general anaesthesia results in respiratory inadequacy and the patient is better off if paralyzed by relaxants and ventilated artificially. This may result in a purposely induced alkalosis. The other more old-fashioned school maintains that the patient may be as well if not better off breathing on his own, provided respiration is not unduly depressed.

For the purpose of this series we allowed our patients to breathe spontaneously. Ventilation studies were carried out on a number of these cases after a steady state of anaesthesia had been established and had been in progress for three or four hours. Tidal and minute volumes were measured and arterial samples taken to determine pH, pCO_2, and blood bicarbonate levels.

Table I shows the results obtained by Dr. Bromage in estimating the minute volume and arterial CO_2 tensions, in fourteen of these patients using a non-rebreathing system. For comparison we have included results in a comparable

TABLE I

SPONTANEOUS RESPIRATION: VENTILATION AND ARTERIAL pCO_2

Technique	No. of Cases	Minute Volume (L.)		Arterial pCO_2	
		Mean	Range	Mean	Range
DLP N_2O (Head and neck)	14	5.17	(3.3–8.0)	49.1	(43.0–55.0)
Epidural Thio. N_2O (Abdominal)	16	5.5	(4.2–8.0)	45.0	(37.0–56.0)
				End tidal pCO_2	
Nunn's Series (1958) Thio. N_2O peth.	26	4.6	(1.95–9.10)	46.3	(36.5–65.5)
Robin *et. al.* (1958) Normal sleep	11	5.86	(3.87–8.41)	44.6	(41.0–49.0)

series of abdominal cases anesthetized with continuous epidural anaesthesia using a thiopentone and nitrous oxide/oxygen supplement. Recently published figures by Nunn (16) showing end-expiratory CO_2 tensions under the conditions designated, and during sleep as established by Robin (17) are also noted.

Figure 2 illustrates in a bicarbonate, pH diagram that the arterial CO_2 tensions in these patients ranged between 43 and 55 mm. Hg.

This available evidence indicates no serious degree of respiratory acidosis. Possible effects of our administrations on metabolic rates can only be speculated on. In addition, certain workers have demonstrated reductions in CO_2 production and a coincidental decrease in oxygen uptake under Fluothane anaesthesia. However, the reasons for this are by no means clear.

CONTROL OF BLOOD LOSS

A conservative attitude has seemed essential in considering the application of induced hypotension to these patients. Experiences have pointed to the potential hazards of prolonged reduction in arterial pressure, particularly as applied to patients in the older age group. Among the older patients in this series, the incidence of hypertensive cardiovascular disease was high. We had no knowledge concerning the degree of atheromatous or medial changes in their arterial systems, and preoperative blood volume determinations were seldom done. Extreme and prolonged degrees of arterial hypotension were therefore avoided. In younger patients with no evidence of vascular or cardiac disease, more active hypotensive methods were used. It was felt that a contribution could be achieved by the

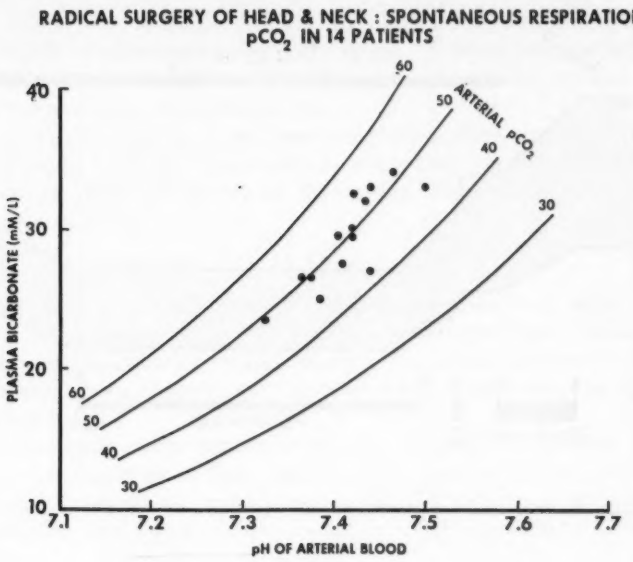

FIGURE 2

application of discreet arterial hypotension for a minimum period of time. The word discreet refers to the maintenance of average levels of arterial pressure in a range of between 80 and 100 mm. Hg in normotensive individuals. In patients suffering from essential hypertension only, the highest levels at which an effective decrease in arterial haemorrhage could be obtained was used.

Elevations in venous pressure are avoided by preventing sudden increases in airway pressure. These may be of mechanical or reflex origin. Posture also assists greatly in the provision of adequate venous drainage of the head and neck as well as being an aid in acquiring the optimal degree of arterial pressure.

Figure 3 shows in a diagrammatic fashion the method used.

(1) The volume of the DLP mixture given varied between 8 and 20 cc. depending on the individual response. It was usually discontinued if the blood pressure reached 90 to 100 mm. Hg or the pulse rate exceeded 96 per minute.

(2) The patient was then postured in a variable degree of a head-up tilt in an attempt to establish a stable arterial tension between 80 and 100 mg. Hg.

(3) If the blood pressure rose during the early part of the operation and arterial bleeding became more active, more hypotension was induced with the use of hexamethonium, thiophanium, or trophanium for minimal effective periods.

(4) If considered preferable, alterations in the concentration of halothane could be depended upon to induce a lesser hypotensive effect. This method appears to us to be very effective, but unfortunately we have no control series with which to compare.

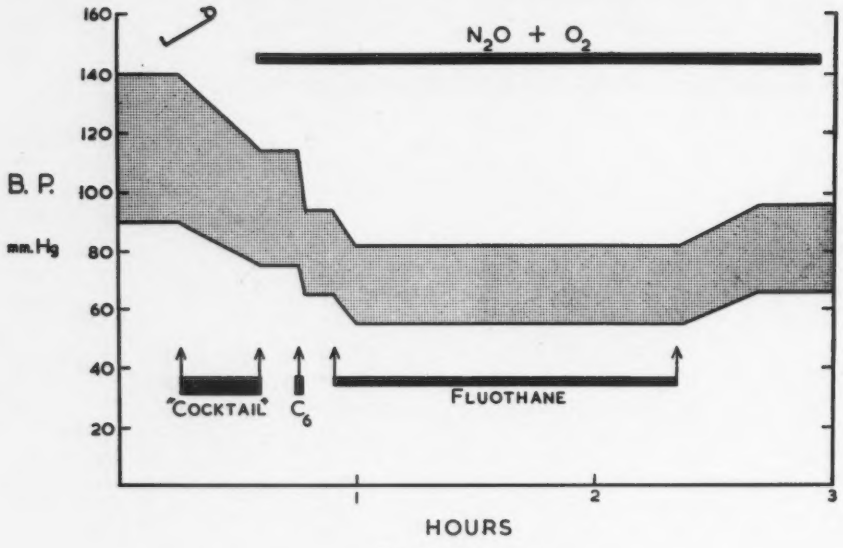

FIGURE 3

Blood loss is routinely measured throughout surgery in a simple and helpful manner. We assumed accuracy within a range of 200 to 400 cc.

(1) Sponges are weighed individually as discarded.

(2) Suction bottles are marked off in units of 100 cc.

(3) If any wet sponges are used, they are moistened in a known volume of saline. This volume is checked before and after the operation.

(4) We estimate the volume of blood on the drapes.

Despite a lack of absolute accuracy, the method is helpful and better than simple guesswork. Its simplicity allows daily application even with frequent changes in operating room personnel.

COMPLICATIONS DURING ANAESTHESIA

In laryngeal cases, if a proliferative neoplasm exists in the vestibule or on one of the cords, the anaesthetist should make a point of inspecting the lesion before commencing anaesthesia. It is important to decide whether or not the lesion can be safely passed by an adequate tube. In performing a nasal intubation, traumatic epistaxis should be considered as an avoidable complication.

If there are obvious hazards to either the induction of general anaesthesia or endotracheal intubation, preoperative tracheotomy under local anaesthesia is indicated. If early tracheotomy is necessary in laryngectomies, invasion of the surgical field by obstructing tracheotomy attachments can be avoided by preparing the laryngeal stoma under local block, and inserting the special right-angled tube before the induction of general anaesthesia.

Once anaesthesia is underway, we are all aware of the problems caused by kinked tubes, a pharynx inadequately sealed off from the trachea by proper packs, or an inadequate inflatable cuff, and the frustrations caused by connections that come loose under the drapes.

Once a tranquil anaesthetic has been established, there are many routine duties to attend to. In neck cases there are two important complications to anticipate. These are: (i) disturbances due to the carotid sinus reflex, and (ii) accidental tension pneumothorax.

Reflex Disturbances

Several types of parasympathetic reflex disturbances may occur. They have not been encountered frequently in these cases. The most important reflex resulted from manipulation of the carotid sinus. In one instance a similar vagal effect resulted from pressure on the pharyngeal plexus deep to the posterior pharyngeal wall.

On three occasions the carotid sinus reflex resulted in a marked bradycardia and hypotension. In all of these instances, the routine preliminary injection of the area with local anaesthetic had been overlooked. All responded to the cessation of the stimulus and the intravenous administration of 1/100 to 1/50 of a grain of atropine.

In one instance marked bradycardia, hypotension, and respiratory depression occurred with stimulation of the active carotid sinus and the condition persisted despite the cessation of stimuli and the use of intravenous atropine. Prompt improvement resulted from the intravenous administration of methedrine 5 mg. and a subsequent carotid sinus infiltration with 1 per cent lignocaine.

A cardiac monitor fitted with a small amplifier is of value in the early identification of these reflexes.

Tension Pneumothorax

We are indebted to Dr. Olga Schweizer and Dr. William Howland of the Memorial Center in New York for the excellent contributions concerning this complication (6). They reported ten cases occurring in their hospital in one year but did not mention the relative incidence. Akin and Smith (19) in 1952 reported eight cases with a 50 per cent mortality. Thomas and Hucks (10) reported four such incidents in thirty-seven radical neck dissections.

We have had three such occurrences in three years. The surgical literature tends to relate the occurrence of this complication to respiratory obstruction, but Schweizer and Howland's explanations are of more value to the anaesthetist. They describe the direct communication of the space between the middle and deep layers of the deep cervical fascia with the superior mediastinum. Mere exposure of the trachea or dissection of the internal jugular vein will open this space. However, the pneumothorax is caused not by the opening of the space, but by air being sucked into the mediastinum by laboured respirations. Trapping occurs with narrowing of the superior mediastinal orifice on expiration. This is shown diagrammatically in Figure 4, and this increasing pressure in the mediastinal pleura may result in a pneumothorax. Mediastinal air under tension may, of

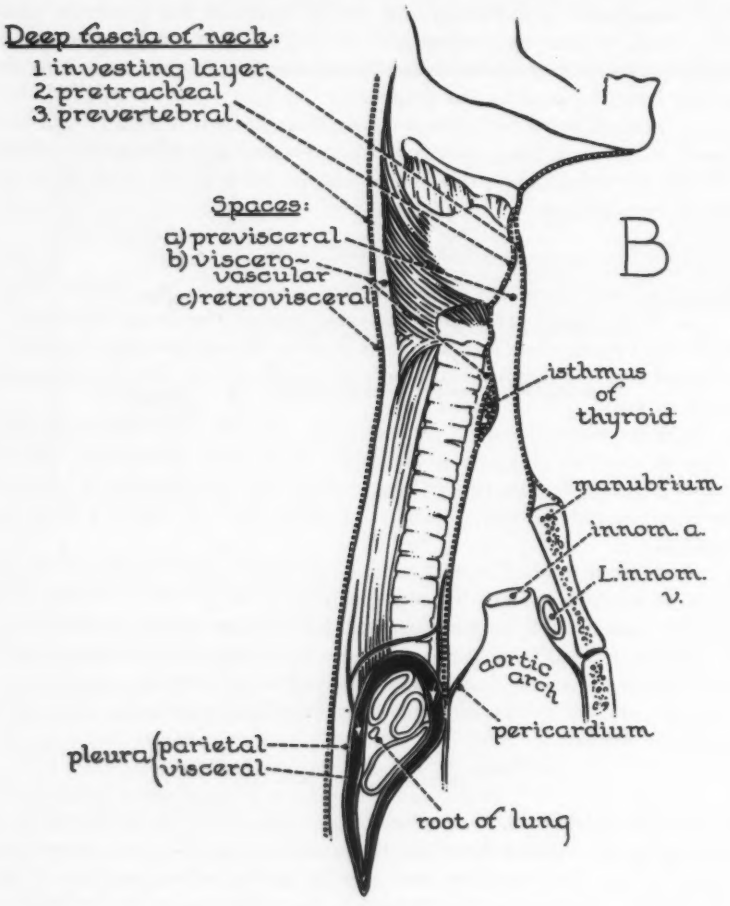

FIGURE 4

course, also dissect into the soft tissues of the neck, face, thoracic wall, and axilla.

In 1954 an incident occurred at the Royal Victoria Hospital of which no one is proud, but it well illustrates the probable train of events if the anaesthetist is not alert to the possibility of this complication.

In his summary of events, the surgeon reported that as he was about to close the incision following radical neck dissection, respirations became laboured and the patient began to buck. He complained to the anaesthetist who remarked that the patient was a bit light. The surgeon proceeded, but the laboured respirations continued and he complained again. This time the anaesthetist remarked

that the tube must be too close to the carina and she adjusted it. There was still no improvement and a few minutes later respirations ceased owing to cardiac arrest. A thoracotomy was performed and within two minutes the heart responded to direct cardiac massage. At this time marked shifting of all mediastinal structures to the left was noted. The right tension pneumothorax was treated by the insertion of a tube and underwater drainage, and radiological examination revealed almost complete expansion of the right lung a few hours later. The patient was maniacal for a few days, but there was no evidence of permanent serious cortical damage afterwards. She is still alive and well.

One of our patients was chronically bronchitic and the 4-hour anaesthetic was disturbed on six occasions by the necessity to aspirate secretions through the endotracheal tube. Towards the end of operation the patient's colour deteriorated, respirations became laboured and inadequate aeration to the right chest was noted. With the establishment of underwater drainage, a considerable amount of air escaped from the chest. The patient's condition improved immediately.

The diagnosis of this complication is easy, particularly if one is aware of the possibility. Laboured respirations, bronchospasm, and a disparity between laboured respiratory excursions and minimal movement of the rebreathing bag occur. As the tension increases, the last sign becomes more obvious. The tachycardia, cyanosis, cardiac arrhythmias, and hypotension are, of course, reflections of the existing hypoxia. The clinical identification of diminished breath sounds, increased resonance, and evidence of mediastinal shift may be inconclusive. One should not wait for radiological confirmation.

Prompt establishment of underwater catheter drainage of the affected pleural cavity will usually result in the expansion of the collapsed lung within a few hours. With prompt diagnosis and proper treatment this accident should not present a serious hazard.

Postoperative Care

The patient should be kept under continual close supervision and nursed in the head-up position. Venous drainage of the head and neck is thereby improved and this position is also of value in the reduction of intracranial pressure.

Postoperative facial cyanosis is common but does not necessarily indicate serious venous obstruction. Schenken *et al.* have postulated that this may be a manifestation of adequate flow of blood from intracranial to extracranial areas with resultant reduction of venous congestion within the cranial vault.

Postoperative tracheotomy should be performed whenever reactive laryngeal oedema might be anticipated and when venous drainage of the neck has been affected bilaterally.

Postoperative increase in intracranial pressure is a potential hazard following removal of the second internal jugular vein or following a simultaneous bilateral neck dissection. The complication occurs occasionally despite the presence of an extensive collateral venous system. Headache, cyanosis, respiratory depression, hypertension, and papilloedema may occur and the diagnosis confirmed by the

finding of a marked increase in spinal fluid pressure. This complication did not occur in any of our cases.

Summary

A non-rebreathing technique is useful in maxillo-facial and radical neck surgery because it enables adequate control with the anaesthetist and his equipment well isolated from the surgical field. With the method described there appears to be some decrease in spontaneous ventilation, but severe respiratory acidosis does not occur. Efforts to produce a moderate reduction in arterial pressure, and the avoidance of increases in venous pressure are of definite value in minimizing blood loss. Certain complications must be continuously anticipated.

In many cases postoperative tracheotomy is required to prevent respiratory obstruction in the postoperative period. The routine use of a head-up position is an important aspect of postoperative care.

Acknowledgments

The author wishes to express gratitude to Dr. Philip Bromage who conducted the ventilation studies and acted as friendly critic during revisions of this paper. Dr. E. J. Tabah of the Department of Surgery, Royal Victoria Hospital, was the tolerant surgical consultant.

Résumé

Au cours de la chirurgie qui se pratique sur la tête et le cou, il faut habituellement une anesthésie de longue durée et bien calme.

Pour arriver à cette fin, nous employons une technique sans réinspiration; ce système, tout en permettant à l'anesthésiste de conserver un bon contrôle sur le malade, isole l'anesthésiste et son matériel du champ opératoire. A part cela, nous suivons habituellement la ligne de conduite suivante: induction avec Phénergan, Largactil et Demerol, intubation après injection de curare si nécessaire, mais après anesthésie locale systématique; le maintien de l'anesthésie se fait avec du protoxyde d'azote ajouté ou associé à un autre agent anesthésique. Ainsi anesthésié, le malade conserve son rythme respiratoire. S'il survient de l'hypoventilation et de l'acidose respiratoire dans ces circonstances, ce n'est rien de très marqué.

Pour diminuer les pertes sanguines, une légère hypotension artérielle est toujours efficace de même qu'une tension veineuse dans les limites de la normale.

Il peut survenir certaines complications, telles: l'obstruction des voies respiratoires par une tumeur, un réflexe du sinus carotidien ou un pneumothorax. L'anesthésiste doit essayer de prévenir ces ennuis et les diagnostiquer précocement s'ils surviennent.

Au cours des suites opératoires, il s'impose de laisser la tête élevée. Dans bien des cas, comme mesure préventive de l'obstruction respiratoire, nous suggérons fortement la trachéotomie.

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THE ROUTINE USE OF LUMBAR EPIDURAL ANAESTHESIA IN OBSTETRICS: A CLINICAL REVIEW OF 9,532 CASES

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IN OUR SOCIETY, modern woman has learned to expect relief of pain in childbirth. Unfortunately, obstetrical anaesthesia is responsible for a significant proportion of maternal deaths (1). Most of these deaths are due to aspiration of vomited or regurgitated stomach contents (2, 3). This accident occurs in the best hospitals despite the training and skill of qualified anaesthetists.

To solve this problem regional anaesthesia has often been suggested, but for various reasons it has never become universally popular. Low spinal anaesthesia (saddle-block) has been used in some centres for years. Unfortunately, in many centres, the high incidence of post-spinal headaches (4, 5) and some reported serious neurological sequellae (6) have caused it to be shunned by both obstetricians and the public. Pudendal block has been tried, but results have not been consistently good enough to warrant its universal adoption. Recently, several reports (7, 8) have appeared in the literature on the use of lumbar epidural anaesthesia in obstetrics. Results appear to be good, but for several reasons the method has been used on only a fraction of the patients delivered in any centre.

Our purpose at this hospital was to investigate the possibility of establishing lumbar epidural anaesthesia as the routine method for relieving pain in childbirth. By routine, we mean that, except when contraindications existed, all mothers would receive this type of anaesthetic for their delivery.

We would not be satisfied with only selected cases, or cases with special indications being anaesthetized in this way. If only 50 per cent of cases are delivered under epidural anaesthesia, we have only reduced the hazards of inhalation anaesthesia by 50 per cent. This we did not consider good enough.

The following reasons are considered by us as contraindications to this method of anaesthesia: (1) refusal of patient to accept this type of anaesthesia; (2) infection of the back area; (3) certain neurological conditions; (4) certain abnormalities of the spinal column; (5) patients with bleeding tendencies or on anticoagulant therapy.

On analysis we found several factors existed which opposed the routine adoption of epidural anaesthesia. We will outline these factors and indicate how they were dealt with in our hospital.

1. *Objections of obstetricians.* In common with other physicians, obstetricians are inherently suspicious of new methods. They cling to established procedures and require special indications before allowing something new to be tried on their patients. This not only prevents the adoption of any new technique as a

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routine, but also prevents the anaesthetists from using the new technique frequently enough to become proficient in its use. In the period from September, 1953, to October, 1956, inhalation anaesthesia was the routine method used in our hospital for obstetrics. During this period we had three women in whom aspiration of stomach contents occurred. All three were fortunately saved by timely and intensive treatment, but all three were very close to death. Combined meetings were held of the staffs in obstetrics and anaesthesia to discuss these near deaths. It was agreed that if future catastrophes were to be averted, some alternative to inhalation anaesthesia in obstetrics must be found. Our obstetrical staff was, therefore, entirely co-operative in allowing us to practise epidural anaesthesia on all their patients and they were very sympathetic during the early period while we were learning the technique. Furthermore, because we used this new method on all patients we soon became quite proficient.

2. *Opposition of anaesthetists.* Anaesthetists, too, are reluctant to replace a method in which they have become proficient over the years, with a new technique which requires learning, and in which at first they will exhibit some clumsiness. It was realized that in the early period a few anaesthetic failures, or even one serious complication might spell the doom of the new technique. It was, therefore, decided that in the first week, only the chief of the anaesthetic staff would attempt epidural anaesthesia in the obstetrical cases assigned to him. After this period, he found that the method was not difficult and that of 24 attempted epidurals, 24 successful blocks had been obtained without any apparent complications. In every instance, both obstetrician and patient were pleased. The result of his experiences was then reported to the members of the anaesthetic staff, and it was decided to adopt lumbar epidural anaesthesia as the routine method for obstetrics. In some instances this was done reluctantly at first, but very soon all members were using this method by preference.

3. *Objections of the nursing staffs.* Like doctors, nurses are inherently opposed to any changes in routine. In the case of epidural anaesthesia several changes were necessary. The nurses had to watch the patients more carefully during labour to allow time for an epidural block. In addition they had to provide a sterile tray and had to position the patient on the table for the procedure. This was done very reluctantly at first. They soon realized, however, that the new technique had advantages. They were spared the emptying of emesis basins at the termination of the anaesthetic and they soon appreciated the advantage to both mother and baby. The nursing staff at our hospital is now enthusiastic about epidural anaesthesia in obstetrics.

4. *Opposition of patients.* In this centre, many patients usually dread spinal anaesthesia. At the beginning we therefore had to emphasize the fact that this was not a spinal anesthetic. We explained that although this technique meant a "needle in the back," this needle was not introduced as far as it was with a spinal anaesthetic, and that headaches would not result. In addition, most mothers had at first expressed a preference for "going to sleep, so that they would not see what goes on." We explained that they would experience a tremendous thrill when they heard their baby cry as soon as it was born. These first patients were so pleased with their epidural anaesthetic that they told their friends, and soon

patients arrived asking for this new type of "needle anaesthetic." Now we seldom have a patient who objects. We never force an epidural anaesthetic on a patient who does not agree to have one.

5. *Problems in technique.* The technique of lumbar epidural anaesthesia (9) as described by previous authors requires an appreciable period of time. Since the exact time of delivery is not predictable, it was apparent at the start that to include all cases, the accepted techniques of epidural anaesthesia would have to be modified so that a block could be performed very quickly. We will, therefore, describe our present technique which we believe has much to recommend it, and which has proved to be entirely safe.

(*a*) *Scrub.* Most authors recommend that the anaesthetist scrub his hands for from 5 to 10 min. and then carefully don a sterile gown and gloves. In this interval a quick multipara might deliver her baby without the advantage of an anaesthetic, or the anaesthetist might have to abandon his scrub and quickly place a mask over her face. In this hospital we neither scrub nor gown. We do, however, wear a cap and mask and put on a pair of sterile rubber gloves, a procedure which requires only a few seconds. In view of the fact that a surgical scrub is deliberately omitted, we are particularly meticulous in putting on our sterile rubber gloves. We realize that we may be criticized for inviting infection, but in our 9,532 obstetrical cases and 5,091 surgical cases not a single infection has occurred. To us it appears that inhalation anaesthesia presents a far greater hazard.

(*b*) *Preparation of back.* At first we used coloured alcoholic solutions of the popular antiseptics. A few mild skin reactions occurred in the first few months. We changed to Cetavlon ® (a detergent), and have used it exclusively since then. The Cetavlon is rubbed on the back for a few seconds. The back is then dried rapidly with sterile gauze. This drying is important because: (i) it is undesirable to introduce detergent into the epidural space and cause possible nerve damage (9), and (ii) detergent renders the gloves slippery and makes handling of the epidural needle more difficult. As stated previously, the lack of infection has proved this skin preparation entirely satisfactory.

(*c*) *Method of finding epidural space.* Most authors recommend the "change in resistance" (9) technique with either air or fluid in the syringe. A few recommend the "hanging drop" method, and a very few recommend the "touch" method. Our method combines features of all these three previously recommended methods. After a preliminary skin wheal over the interspace between L3–L4 or L4–L5, a 16- or 17-gauge Tuohy needle is introduced into the interspinous ligaments. A 20 cc. syringe filled with lidocaine 2 per cent (Xylocaine) is attached, and the resistance to injection is felt. This manœuvre also provides a drop of fluid in the hub of the needle. Some of our staff anaesthetists omit this step, and instead fill the hub from the syringe to which a hypodermic needle is attached. With the syringe detached from the Tuohy needle, the hub of the needle is grasped between the thumb and index fingers of the right hand. The ulnar side of the left hand is then placed against the patient's back, and the shaft of the needle is held between the thumb and fingers of the left hand. The left hand is used to guide the needle in the proper direction, and to prevent too

rapid or jerky advance of the needle by the right hand. One soon learns to judge (by sense of touch) when the thick ligamentum flavum is reached, and then it is pierced with a steady pressure. In over 80 per cent of cases the drop of fluid in the needle hub is now sucked in, and thus announces that the epidural space has been reached. In the other 20 per cent of cases one's sense of touch makes the same announcement. In either case the syringeful of lidocaine is now connected to the needle, and the lack of resistance to injection corroborates the proper placement of the needle. There is no test dose and no waiting period. Time cannot be spared. Should the dura be inadvertently punctured, our large needles provide a rapid outward flow of spinal fluid to give us due warning. The large size and shape (Huber point) of the Tuohy needle makes it very easy to deviate to one or other side of the mid-line. With practice this tendency can be corrected. However, if this does occur and the lamina is reached instead of the ligamentum flavum, valuable information has been gained, because the depth of the ligamentum flavum has been indicated for that particular patient. Slight redirection of the needle will find the ligamentum flavum and the epidural space.

Using this technique the members of our staff can usually introduce a needle into the epidural space within three minutes of entering the delivery room. In a very few patients, because of anatomical difficulties, it occasionally takes longer, but this occurs only rarely.

(*d*) *Timing.* An important feature that must be learned is at what stage in labour to begin the epidural anaesthetic. If given too soon, the anaesthetic will wear off before the patient delivers, and necessitate the repetition of the anaesthetic. This does no harm, but the patient is subjected to a second needle, and the obstetrician may become suspicious that the anaesthetic has slowed the progress of labour. On the other hand, waiting too long may not give the epidural time enough to give complete relief of pain before the patient delivers. Obviously as one becomes more experienced in the method, the procedure takes less time, and one can wait until later in the course of labour before proceeding with the anaesthetic. With primiparas we wait not only until caput is visible, but until caput is well down on the perineum. These patients will rarely precipitate. An obstetrician who wishes to save the patient some suffering may request an earlier anaesthetic, but in this instance he may have to apply forceps. Patients are able to bear down after they receive an epidural anaesthetic, and some of them do so very effectively if requested. However, the anaesthetic does inhibit the urge to push, and an unco-operative patient will not do so.

Multiparas present more of a problem. We have found that a more important criterion exists than the degree of dilatation of the cervix, namely the degree of descent of the head (or station). With the head at the ischial spines or above, even with full cervical dilatation, it may take two hours or more before the patient is ready for delivery. On the other hand, we have administered epidural anaesthetics to patients with only 4 cm. dilatation when the head had descended to station 2 plus or lower, and have then found that the cervix has rapidly "melted away" soon after the epidural was given, and that the patient was ready for delivery in a few minutes. In the last analysis, judgment as to when to give the epidural is an individual problem, and can only be learned after much

experience. After introducing the lidocaine into the epidural space, the pains of the contractions disappear in 3 to 4 min. However, it usually takes 10 to 15 min. for full perineal anaesthesia to develop. We have found it profitable to administer an epidural anaesthetic in cases when it is quite obvious that the patient will not wait 10 to 15 min. for delivery. Nitrous oxide or cyclopropane administered only to the stage of analgesia during delivery of the head will render childbirth painless. The epidural will be effective for the repair of the episiotomy or laceration. We have never seen vomiting or regurgitation occur with an inhalation anaesthetic of such short duration.

Results

Our purpose, as stated previously, was to investigate the possibility of establishing lumbar epidural anaesthesia as the routine method for vaginal deliveries. From the table it may be seen that in September, 1956, the month before we

TABLE I
Results

	Vaginal deliveries								Caesarean sections		
	Total	Epidural	(%)	General	(%)	Local	Spinal	Nil	Spinal	Epidural	General
Sept., 1956	313	0	0	277	89.9	1	23	12	16	0	3
Oct.	306	105	39.3	185	60.4	2	8	6	16	3	0
Nov.	303	150	49.6	144	47.6	3	2	4	5	9	2
Dec.	294	198	67.3	89	30.2	3	1	3	9	7	0
Jan., 1957	265	196	74.0	57	21.5	0	3	9	5	9	0
Feb.	270	204	75.5	52	19.3	4	1	9	8	4	1
March	335	276	82.4	49	14.6	3	3	4	8	4	0
April	309	241	78.0	45	14.6	1	10	12	13	4	0
May	322	273	84.8	37	11.5	3	4	5	22	2	0
June	325	285	87.7	30	9.2	2	3	5	11	5	1
July	322	285	88.5	27	8.4	3	1	6	6	3	0
Aug.	295	251	85.0	33	11.2	3	6	2	6	4	1
Sept.	295	261	88.5	31	10.5	2	1	16	9	3	1
Oct.	300	269	89.5	22	7.3	2	4	3	22	3	2
Nov.	300	274	91.5	17	5.7	0	2	7	14	2	3
Dec.	265	236	89.0	22	8.3	0	4	3	14	8	2
Jan., 1958	304	282	93.0	13	4.3	3	2	4	10	2	1
Feb.	267	242	90.6	16	6.0	2	0	7	7	2	0
March	309	288	92.5	12	3.9	3	1	5	8	7	0
April	301	278	92.5	16	5.3	1	0	6	5	5	0
May	279	252	90.4	14	5.0	5	0	8	11	14	0
June	301	277	92.0	14	4.6	2	4	4	7	6	0
July	297	269	90.6	13	4.4	2	4	9	12	8	0
Aug.	262	229	87.5	25	9.6	3	1	4	6	6	1
Sept.	263	236	89.8	14	5.3	5	4	4	14	7	0
Oct.	289	263	91.0	16	5.5	2	1	7	6	16	2
Nov.	252	232	92.0	13	5.0	1	1	5	1	6	1
Dec.	288	263	91.5	15	5.2	3	0	7	2	12	0
Jan., 1959	291	255	87.8	15	5.2	5	3	13	11	11	0
Feb.	255	230	90.3	13	5.1	7	0	5	1	12	0
March	333	306	91.7	14	4.2	2	2	9	1	21	0
April	307	292	95.2	11	3.6	2	0	2	2	17	0
May	327	307	94.0	10	3.0	3	1	6	3	1	1
June	329	297	90.3	23	7.0	1	5	3	0	15	0
July	338	315	93.2	15	4.4	2	1	5	0	12	0
Aug.	332	312	93.5	11	3.3	0	1	10	0	10	0
Sept.	355	327	92.1	18	5.5	1	3	6	2	16	1

Total epidural anaesthetics: 9,532—9,256 vaginal deliveries; 276 Caesarean sections.

began practising this method, general anaesthesia was used in 89.9 per cent of cases. Within six months, lumbar epidural anaesthesia was being used for about 80 per cent of vaginal deliveries, and general anaesthesia for about only 15 per cent. After one year, epidural anaesthesia was being used in 90 per cent of cases and general anaesthesia in less than 10 per cent. We now find that general anaesthesia is only used in about 5 per cent of cases.

Complications

The two most classically dreaded complications in epidural anaesthesia are: massive or total spinal anaesthesia (10, 11), and convulsions (10, 11).

Massive or Total Spinal Anaesthesia

This occurred four times in our 9,532 cases, or 0.04 per cent. It is caused by the addition of a large volume of local anaesthetic drug to the spinal fluid in the subarachnoid space. Our use of large gauge needles for epidural anaesthesia helps to warn us if the dura is accidentally punctured. At first it was our practice to proceed with epidural anaesthesia in another interspace when the dura was accidentally punctured. However, in the early months of our experience, two cases of massive spinal anaesthesia resulted on successive days when this was done. Since then it is our practice to abandon lumbar epidural anaesthesia if inadvertent dural puncture occurs. Instead, we inject 3 to 4 cc. of lidocaine 2 per cent into the spinal fluid and thus purposely administer a spinal anaesthetic.

Two other cases of total spinal anaesthesia occurred in which there was no evidence of dural puncture present to warn us. In all cases the patients rapidly lost consciousness and spontaneous respirations ceased. These patients were immediately ventilated with 100 per cent oxygen. An intravenous infusion was started and vasopressors were given intravenously when indicated. In all instances consciousness and spontaneous respiration was resumed in from 60 to 90 min. There were no adverse effects observed in mother or infant in any of the four instances.

Convulsions

Convulsions occurred six times, or 0.063 per cent. These are a toxic reaction to the local anaesthetic drug. In all cases patients were ventilated with oxygen, with either a face mask or an endotracheal tube. Succinylcholine and/or intravenous barbiturate were given if adequate oxygenation was not possible because of convulsions. All convulsions were controlled within 5 min. None of the six mothers and infants showed any deleterious effects whatsoever.

It is gratifying that these dreaded complications occurred so infrequently, and that when they did occur, they all responded so favourably to treatment.

We wish to stress, however, that these complications can and do occur. For this reason lumbar epidural anaesthesia should never be attempted by the untrained or occasional anaesthetist, who is not able to treat these complications.

Less Serious Complications

Hypotension. This occurs more gradually and is usually of a lesser degree than the hypotension associated with spinal anaesthesia. We have decreased its incidence by routinely placing the patient's legs up in stirrups immediately after the drug is injected into the epidural space. Despite this manœuvre nearly all cases experience a slight blood pressure drop, usually of about 10–20 mm. mercury. We do not administer a vasopressor drug unless the systolic blood pressure falls below 80 mm. mercury. Neither mother nor infant seems to be adversely affected by hypotension of this degree. We have administered vasopressors 130 times in our 9,532 cases, or 1.363 per cent.

In pre-eclamptic patients who have not responded to routine medical therapy, we have utilized the hypotensive effect of epidural anaesthesia with what appears to be good results. We introduce a vinyl plastic catheter into the epidural space during labour, and give repeated doses of lidocaine 0.5 per cent until the desired degree of hypotension is achieved. When the patient is ready for delivery we introduce lidocaine 2 per cent via the same epidural catheter, to achieve adequate obstetrical anaesthesia.

Drowsiness. This occurs fairly frequently. It is, we believe, in part a toxic manifestation of lidocaine. In other cases it is due to the analgesic and sedative drugs which the patients have received earlier in labour. With relief of pain following the epidural anaesthetic, the sedative effect of these drugs becomes more pronounced and renders the patient drowsy. We have found drowsiness an advantage rather than a disadvantage.

Shivering. A few patients experience intense shivering. We have, however, seen it in some patients before the epidural anaesthetic has been administered. We do not know its significance, but it apparently causes no harm.

Vomiting. This seldom occurs with epidural anaesthesia. When it does occur it may be associated with (*a*) a rapid fall of blood pressure, (*b*) a rapid rise of blood pressure due to the administration of a vasopressor drug, or (*c*) most frequently, after the administration of an ergot derivative. Vomiting has never been severe enough to constitute a problem.

Arrest or slowing of labour. From our observations on this large series, it is our impression that epidural anaesthesia does not interfere with the progress of labour. Good contractions still occur after the anaesthetic has been administered. It is also our impression that dilatation of the cervix is more rapid after an epidural anaesthetic. The desire to bear down does disappear, but a co-operative patient can still push effectively, if so instructed. In the early days of our series, a few epidural anaesthetics were administered to patients in whom full dilatation of the cervix had occurred, but in whom the foetal head had not descended below the level of the ischial spines. In some cases the anaesthetic wore off before the patient was ready for delivery. The obstetricians, in these instances, tended to blame the anaesthetic for slowing the progress of labour. Since then, we have seen many similar cases of patients with full dilatation of the cervix, and a high foetal head. No anaesthetic has been given to these latter patients, yet they were not ready for delivery for two hours or more. We therefore think that the first cases represent improper timing of the anaesthetic, but that no slowing of labour

occurred. A repeated epidural anaesthetic in these cases caused no apparent harm.

Improper timing. This occurred 31 times, or 0.33 per cent. It includes those instances in which the epidural anaesthetic was given too soon and the effect had worn off before the patient was delivered and the perineum repaired.

Inadvertent dural puncture. This has occurred 78 times, or 0.82 per cent. Included in this series are epidural anaesthetics attempted by interns and residents with no previous experience and by members of our staff when they were neophytes in epidural anaesthesia. Dural punctures decrease in frequency with the increasing experience of the anaesthetist in epidural anaesthesia. They will, however, occur to some extent to even the most experienced. We use large bore needles (16 or 17 guage), so that inadvertent dural puncture is usually very evident when it occurs.

Headache. Headaches are encountered very infrequently as sequellae of epidural anaesthesia (11). Most of them occur in conjunction with inadvertent dural puncture. Some cases have occurred, however, where no dural puncture had taken place.

Other neurological sequellae. We have no accurate statistics on these available from our records. We have, however, from the start of this series asked the obstetricians to report these cases to us and they have been very co-operative in doing so. There have been 16 paraesthesias reported, and 9 patients reported who displayed small areas of anaesthesia. These occurred usually over the lateral aspect of the thigh. Most disappeared in three or four days, but in at least two instances they persisted for several weeks. All were transient, and none was serious. We must, however, report a paraplegia which occurred recently following an epidural anaesthetic for surgery (not in this obstetrical series). The paraplegia was rather bizarre in that motor paralysis occurred but no sensory impairment was evident. The patient is making a good recovery.

Infection. It is gratifying that although our technique does not include a surgical scrub of the hands, or donning of a sterile gown, in our 9,532 obstetrical cases and 5,091 surgical cases, not a single case of infection has occurred.

Backache. A few patients have complained of backache following this type of anaesthesia. This complaint is common in obstetrical patients regardless of the type of anaesthesia received.

Impressions

After three years of using lumbar epidural anaesthesia as the routine anaesthetic in obstetrics, our entire obstetrical and anaesthetic staffs are unanimous in their approval. We realize that it has shortcomings but believe it to be the very best anaesthetic for obstetrics available today. It eliminates the threat of maternal death through aspiration of stomach contents. It provides excellent anaesthesia. Precipitate deliveries are reduced in number. Infants are not depressed. In a busy case room a single anaesthetist can cope with the three or four mothers who are suddenly ready for delivery. Complications have been few. Patients love it.

Summary

A report is given of an attempt by the anaesthetic staff of the New Mount Sinai Hospital, Toronto, to evaluate lumbar epidural anaesthesia as a routine anaesthetic in obstetrics. This was done primarily in order to eliminate the threat of maternal mortality through the aspiration of stomach contents. To anaesthetize all obstetrical patients in this manner it was necessary to obtain the full co-operation of the entire obstetrical, anaesthetic, and nursing staffs. It was also necessary to modify the technique of lumbar epidural anaesthesia so that the procedure takes only about three minutes. Surgical scrub of the hands and the donning of a sterile gown have been omitted from the technique, with no evidence of infection in the reported 9,532 obstetrical cases and 5,091 surgical cases. The classically dreaded complication of total spinal anaesthesia occurred four times or 0.42 per cent, and that of convulsions occurred six times or 0.63 per cent. All cases responded to therapy without apparent harm to mother or infant. Lesser complications occurred infrequently and have been discussed in the paper. There were no anaesthetic deaths in this series. Labour is apparently not slowed by epidural anaesthesia and dilatation of the cervix seems to be hastened.

After three years of this experiment, we now use lumbar epidural anaesthesia for over 90 per cent of our vaginal deliveries, and general anaesthesia for less than 5 per cent.

The obstetrical and anaesthetic staffs of our hospital believe that although lumbar epidural anaesthesia in obstetrics has some shortcomings it is the most desirable obstetrical anaesthetic available today.

Résumé

Le personnel du service d'anesthésie de l'hôpital New Mount Sinai, Toronto, présente le résultat d'une tentative d'appréciation de l'usage de routine de l'anesthésie épidurale lombaire en obstétrique. Le premier but de cette pratique a été d'éliminer la mortalité maternelle qui survient à la suite de regurgitation et d'aspiration bronchique du contenu gastrique. Pour réussir à administrer cette anesthésie à toutes les malades, il faut absolument être assuré de la collaboration de tout le personnel obstétrical, anesthésique ou infirmière. De plus, il a fallu modifier la technique anesthésique pour qu'elle ne dépasse pas trois minutes. Le brossage chirurgical des mains et la blouse stérile ont été laissés de côté et, sur 9532 cas d'obstétrique et 5091 cas de chirurgie, on ne nous a pas signalé d'infection. La complication classique d'anesthésie rachidienne totale est survenue quatre fois soit 0.42% et celle de convulsions est survenue six fois soit 0.63%. La thérapeutique appliquée a été efficace et ni la mère ni l'enfant ne porte de sequelle. Des complications de moindre importance ont été observées de temps en temps, on les mentionne dans le travail. Dans cette série, aucune mort n'est survenue. Le travail, selon toute apparence, n'est pas ralenti par l'anesthésie épidurale et la dilatation du col semble accélérée.

Après avoir procédé de cette façon depuis trois ans, nous continuons à employer l'anesthésie épidurale dans 90% de nos accouchements vaginaux et nous employons l'anesthésie générale chez moins de 5% de nos cas.

Le personnel des deux services: d'obstétrique et d'anesthésie de notre hôpital s'accordent à dire que, bien que l'anesthésie épidurale en obstétrique aie quelques inconvénients, elle demeure l'anesthésie obstétricale la plus souhaitable à notre disposition aujourd'hui.

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A LABORATORY AND CLINICAL EVALUATION OF MEPIVACAINE (CARBOCAINE ®)

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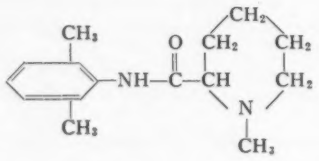
MEPIVACAINE (Carbocaine ®) is a local anaesthetic agent which was described by Ekenstam, Egnér, and Pettersson (1) in 1956. The structural formula of the drug is shown below:



MEPIVACAINE (CARBOCAINE ®)

Mepivacaine is a white, crystalline, odourless powder, melting point 261° C., molecular weight 285.5. The hydrochloride is easily soluble in water, stable in solution, very resistant to acid and alkaline hydrolysis, and can be repeatedly boiled without decomposition.

ACUTE TOXICITY

The acute toxicity of mepivacaine HCl (Carbocaine ®) was compared with that of lidocaine by subcutaneous administration in rats and mice. (Table I, Figure 1.) Isotonic saline was used as the diluent. The volume of injection to body weight for each animal was kept constant at 10 ml./kg. of the various concentrations of both local anaesthetic agents. However, the majority of rats surviving doses of both drugs above the LD_{50} developed skin sloughs at the site of injection. None of the mice developed lesions.

Male mice between 20 and 30 gm. were used. The rats were females between 200 and 300 gm. The absolute volume of injection was consequently greater in the rats although the drug concentration at the various dosage levels was the same in both species.

NOTE. The subcutaneous LD_{50} values for mepivacaine and lidocaine are indistinguishable statistically in both the mouse and the rat. However, the log dose : probit response slope is slightly greater with lidocaine in both species

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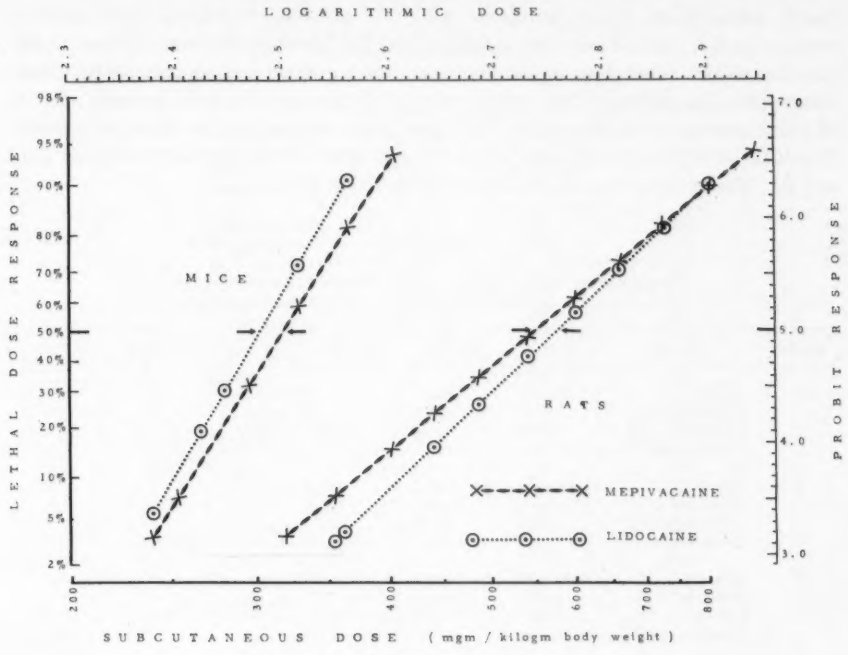

FIGURE 1

TABLE I

ACUTE TOXICITY OF MEPIVACAINE HCl COMPARED WITH LIDOCAINE HCl (SUBCUTANEOUS ADMINISTRATION IN MICE AND RATS)

Species	Number of animals	Sex	Mepivacaine HCl		Lidocaine HCl	
			LD_{50} ± stn. dev. in mg./kg.	Slope	LD_{50} ± stn. dev. in mg./kg.	Slope
Mouse	120	Male	318±21	14.82	301±20	16.04
Rat	200	Female	548±48	7.73	574±49	9.00

(Figure 1). The animals receiving subcutaneous lidocaine were observed to die more quickly than those receiving mepivacaine.

DURATION, SPREAD, AND TISSUE REACTION

The duration, spread of anaesthesia, and tissue reaction with mepivacaine (Carbocaine ®) were compared with procaine and lidocaine in five subjects in standard skin wheals on the volar surface of the forearm. Each drug was injected in 1 per cent solution in isotonic saline, and saline alone was used as a control in a

fourth wheal. Each wheal contained 0.1 cc. of solution. Injections were made in random order, and neither the subjects nor the investigator were aware of the identity of the substances injected at each site until the observations had been completed. Anaesthesia was tested with a hypodermic needle at each site at 15 min. intervals until the prick of the needle was appreciated as sharp or painful. Absolute anaesthesia was recorded as (++), appreciation of touch without pain as (+). These observations are recorded in Table II.

TABLE II

DURATION OF ANAESTHESIA WITH INTRACUTANEOUS WHEALS
(SOLUTION 0.1 CC. OF 1 PER CENT IN SALINE IN EACH CASE)

Subject	Drug	15 min.	30 min.	45 min.	60 min.	75 min.	90 min.
1	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	+	+	—	—	—
	Carbocaine 1%	++	++	++	++	+	—
2	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	+	+	—	—	—
	Carbocaine 1%	++	++	++	++	+	—
3	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	+	—	—	—	—
	Carbocaine 1%	++	+	—	—	—	—
4	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	++	+	—	—	—
	Carbocaine 1%	++	++	++	+	—	—
5	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	++	+	—	—	—
	Carbocaine 1%	++	++	++	+	—	—

The maximum diameter of the area of anaesthesia produced by the standard intracutaneous wheal was also noted in each case, as was the reaction of the tissue as indicated by flare formation or erythema. The results in the five subjects are recorded in Table III.

From these observations it appears that mepivacaine (Carbocaine ®) has a significantly longer duration of action than lidocaine, and several times the duration of procaine, in equal concentration. In four subjects of the five tested, the spreading power of mepivacaine exceeded that of procaine or lidocaine. Of the three drugs tested, procaine alone produced any signs of tissue reaction.

CLINICAL USE

Mepivacaine (Carbocaine ®) has been employed for regional anaesthesia in 230 patients, as shown in Table IV.

TABLE III

SPREAD OF ANAESTHESIA AND TISSUE REACTION FROM INTRACUTANEOUS WHEALS

Subject	Drug	Maximum area of anaesthesia	Tissue reaction	
			Immediate	Late
1	Saline	Nil	Nil	Nil
	Procaine 1%	0.6 cm.	Flare 2x wheal	Nil
	Lidocaine 1%	1.0 cm.	Nil	Nil
	Carbocaine 1%	1.8 cm.	Nil	Nil
2	Saline	Nil	Nil	Ni
	Procaine 1%	0.6 cm.	Flare	Nil
	Lidocaine 1%	1.0 cm.	Nil	Nil
	Carbocaine 1%	2.0 cm.	Nil	Nil
3	Saline	Nil	Nil	Nil
	Procaine 1%	0.7 cm.	Flare	Nil
	Lidocaine 1%	1.0 cm.	Nil	Nil
	Carbocaine 1%	1.0 cm.	Nil	Nil
4	Saline	Nil	Nil	Nil
	Procaine 1%	0.7 cm	Flare	Nil
	Lidocaine 1%	1.2 cm	Nil	Nil
	Carbocaine 1%	2.3 cm.	Nil	Nil
5	Saline	Nil	Nil	Nil
	Procaine 1%	0.8 cm.	Erythema	Nil
	Lidocaine 1%	1.5 cm.	Nil	Nil
	Carbocaine 1%	2.8 cm.	Nil	Nil

TABLE IV

Epidural block	
Lumbar	180
Caudal	3
Brachial plexus block	5
Paravertebral block (somatic)	6
Obturator block (bilateral)	1
Ankle block (anterior and posterior tibial)	1
Maxillary block	2
Stellate ganglion block	20
Lumbar sympathetic block	12
TOTAL	230

MATERIAL USED

Mepivacaine (Carbocaine ®) was used in 2 per cent solution in isotonic saline solution for epidural anaesthesia and peripheral somatic nerve blocks, and in 1 per cent solution and ½ per cent solution in saline for sympathetic blocks (stellate ganglion and lumbar sympathetic chain). The 2 per cent solution was re-autoclaved in the hospital before use.

RESULTS

Epidural Anaesthesia

The most common use of regional anaesthesia in the authors' practice is epidural anaesthesia for the obstetrical patient, the induction of anaesthesia

being delayed until the patient is judged to be ready for delivery. Of the 180 epidural anaesthetics by the lumbar route included in this study, 165 were given for vaginal delivery of obstetrical patients and 15 for Caesarean section. Of the patients delivered per vaginum, 16.5 per cent delivered spontaneously, while 83.5 per cent were delivered by forceps. The obstetricians prefer generally to control the head at the outlet by forceps. This accounts for the large proportion of forceps deliveries in this series.

Onset of Analgesia in Epidural Block

The time to onset of analgesia measured from the time of injection of 2 per cent mepivacaine (Carbocaine ®) in saline was recorded in 90 patients having epidural anaesthesia for obstetrical procedures. The range was from 3 to 23 min., with 96 per cent occurring between 3 and 15 min., and 74.7 per cent in the first 10 min. We have noted that the transition from no anaesthesia to complete analgesia appears in most instances to be quite sudden.

Duration of Anaesthesia in Epidural Block

The duration of anaesthesia after the establishment of epidural block was determined in 63 obstetrical patients. The end-point used was the appreciation of the sharpness of a hypodermic needle or pain on pinching the skin. The shortest period of analgesia was 55 min. and the longest was 220 min.: 63.5 per cent of patients had a duration between 90 and 135 min. ($1\frac{1}{2}$ hrs. to $2\frac{1}{4}$ hrs.), while 53.9 per cent lasted 120 min. (2 hrs.) or more.

Spread of Anaesthesia in Epidural Block

The volume of solution injected into the epidural space in the obstetrical patients studied in this series varied from 13 cc. to 20 cc. Sites of injection were the interspaces between the third and fourth or the fourth and fifth lumbar vertebrae. The spread of anaesthesia varied from two segments above the site of injection to 13 segments above (second thoracic segment). Only three patients received volumes under 15 cc. In 68.1 per cent of those receiving 15 cc. or more, the upper limit of anaesthesia was between 5 and 8 segments above the point of injection. There did not appear to be any fixed relationship between volume injected and level of anaesthesia through this range. We believe this is due to factors for which we have not been able to account, such as rate and force of injection, the influence of uterine contractions and straining in the patient in labour.

Hypotension in Epidural Block

The occurrence of hypotension during epidural block with mepivacaine (Carbocaine ®) 2 per cent was examined in 147 obstetrical patients in which the records were considered adequate for evaluation. Of these, 132 were delivered per vaginum, and 15 were Caesarean sections. Of these, 16 (12.1 per cent) of the patients for vaginal delivery and 9 (60 per cent) of the Caesarean sections

showed a drop of 20 mm. Hg or more in systolic blood pressure before delivery. Four of the patients for vaginal delivery and six of the Caesarean sections received vasopressor drugs to reverse the hypotension. The higher proportion of Caesarean section patients requiring vasopressor drugs is due to the sympathetic paralysis associated with the higher levels of anaesthesia required for this operation.

Sympathetic Blocks

Twenty stellate ganglion blocks and twelve blocks of the lumbar sympathetic chain were done for diagnostic or therapeutic indications. Mepivacaine (Carbocaine ®) in 1 per cent solution was used in ten of the stellate blocks and in two of the lumbar sympathetic blocks, 0.5 per cent solution in saline being employed for the remainder. The use of 1 per cent solution in blocks of the lumbar sympathetic chain resulted in prolonged "overflow" blocking of somatic roots, which lasted for more than two hours. The 0.5 per cent solution proved to be equally effective in producing prompt sympathetic blocks, without overflow effect on the somatic roots. No complications occurred in any of these patients.

Other Somatic Nerve Blocks

The number of patients in whom mepivacaine (Carbocaine ®) has been used in regional anaesthesia other than epidural block and sympathetic block is as yet too small for analysis. It may be noted, however, that in each case in which it has been employed (see Table IV) it has proved to be a satisfactory agent, having a prolonged action without the addition of vasoconstrictor substances. The solution used has been 2 per cent saline.

Summary and Conclusions

The acute toxicities of mepivacaine (Carbocaine ®) and lidocaine as determined by the subcutaneous LD_{50} in rats and mice are indistinguishable statistically although the log dose : probit response slope is slightly greater with lidocaine in both species.

Comparison of 1 per cent solutions of mepivacaine, lidocaine, and procaine in standard skin wheals showed that anesthesia produced by mepivacine lasted three to four times as long as that obtained with procaine, and 50 per cent longer than that produced by lidocaine, while the maximum area of anaesthesia was significantly greater with mepivacaine than with the other two drugs.

Experience with mepivacaine as a local anaesthetic agent in 230 patients has demonstrated that it produces satisfactory and prolonged anaesthesia without the necessity of adding vasoconstrictor substances to the solution. Of the 230 patients recorded in this study, 183 received epidural blocks. Onset of anaesthesia is rapid and no toxic manifestations or evidences of tissue irritation have been seen.

ACKNOWLEDGMENTS

The mepivacaine employed has been generously supplied by Winthrop Laboratories under the trade name "Carbocaine."

We gratefully acknowledge the help of those members of the Department of Anaesthesia of the Toronto General Hospital who have assisted in the clinical studies here reported.

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FLAMMABILITY OF AN AZEOTROPIC MIXTURE OF ETHER AND FLUOTHANE WHEN VAPORIZED IN OXYGEN OR AIR[1]

G. K. BROWN[2]

AN ANAESTHETIC consisting of an azeotropic mixture of ether and Fluothane has been developed in Canada with hopes that it will not be explosive in the concentrations used during anaesthesia procedures. In this respect it is important to know whether the vapour of the anaesthetic is flammable when mixed with oxygen or air and, if so, what the range of flammability is.

As the result of a request received in the summer of 1959 from Dr. Gordon M. Wyant, F.F.A.R.C.S., Professor of Anaesthesia, University Hospital, University of Saskatchewan, Saskatoon, Sask., the Mines Branch of the Department of Mines and Technical Surveys, at Ottawa, agreed to prepare apparatus and perform tests in its electric equipment certification laboratories to determine the flammability limits of a sample of the azeotropic mixture of ether and Fluothane prepared by the manufacturing pharmacy of the University of Saskatchewan.

The flammability limits are not constants but are related to a number of factors connected with the experimental methods of making the determination. Some of these factors are: direction of flame propagation, size and shape of the confining vessel, initial temperature and pressure, turbulence, and source of ignition.

A study of available literature indicates that the lowest lower limit can be obtained with upward propagation of the flame; that normal variations of temperature, atmospheric pressure, and humidity do not have a great effect on the lower limit; that the igniting source should be strong enough to ensure ignition; and that the confining vessel should be long enough that true propagation can be differentiated from local combustion near the ignition source. In tests with tubes (1, 2), the lower limit falls and the upper limit rises as the tube diameter increases, but an increase in diameter beyond about 5 cm. generally has little effect on the limit values.

From a safety point of view the method which will give the widest flammable range is considered the best one to use.

DETAILS OF INVESTIGATION

The apparatus used is illustrated in Figures 1 and 2. It is essentially the same as apparatus used by the United States Bureau of Mines and described in its

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[1]Prepared for publication in the *Canadian Anaesthetists' Society Journal*, July, 1960, by permission of the Director, Mines Branch, Department of Mines and Technical Surveys, Ottawa, Canada.

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SOURCE: Internal Report FMP-60/13-EEC (E.E.C. No. 27), Jan. 28, 1960.

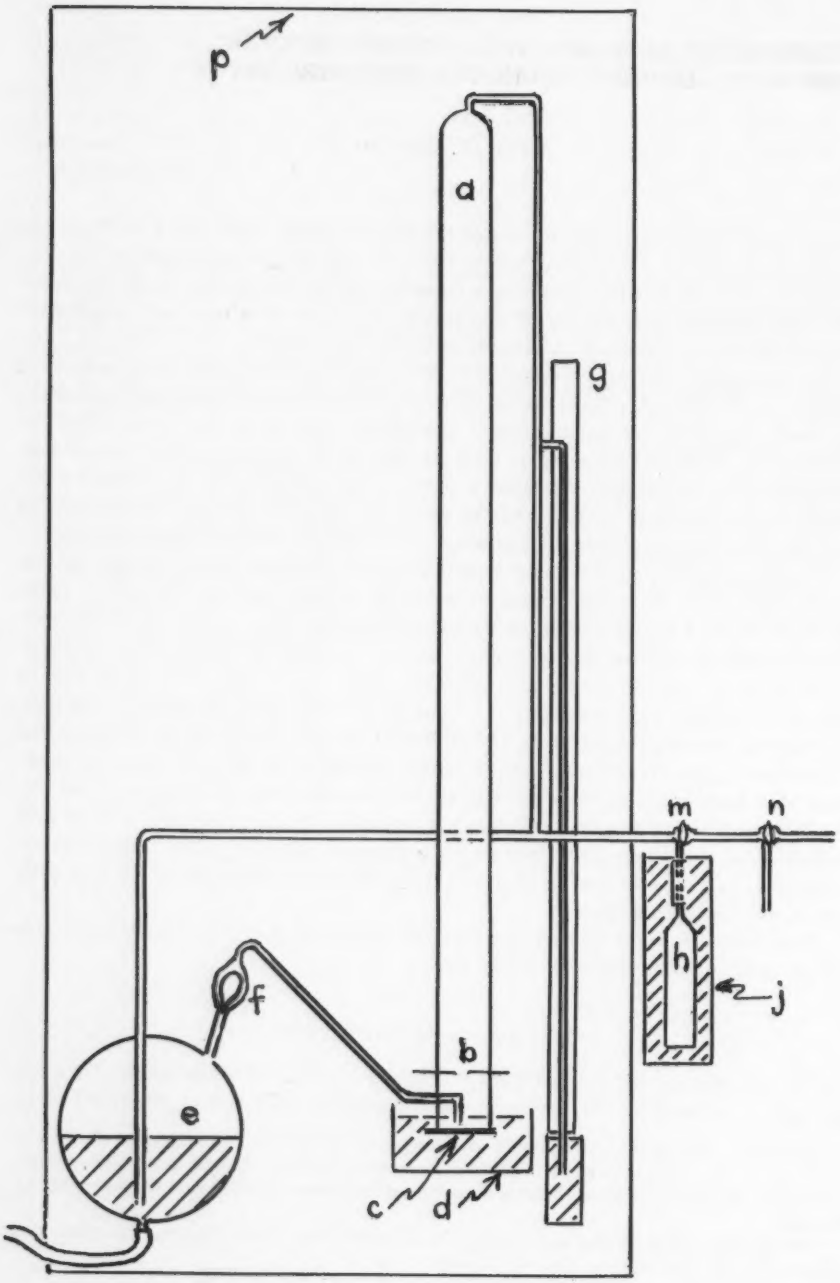
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FIGURE 2. Photograph of apparatus.

Bulletin 503, "Limits of Flammability of Gases and Vapors," except that drying tubes were dispensed with and an over-all enclosure with heaters and fan was provided so that tests could be performed at elevated temperatures.

The principal component of the apparatus consisted of a vertical glass tube 5 ft. long and 2 in. in diameter. Mixtures were prepared in this tube by the partial pressure method; that is, the system was evacuated, anaesthetic vapour was admitted to provide the desired percentage of atmospheric pressure, and oxygen or air was admitted to bring the pressure inside the system back to atmospheric. The mixture was then circulated by means of a pump consisting of a mercury vessel and a one-way valve. Raising and lowering the level of the mercury drew mixture from the top of the tube and pushed mixture in at the bottom. It was found that about twenty cycles of the pump were necessary to ensure

FIGURE 1. Diagram of apparatus

a. Glass tube, 2 in. dia., 5 ft. long
b. Ignition electrodes
c. Ground glass disc
d. Mercury seal
e. Mercury pump
f. 1-way valve
g. Manometer scale
h. Test sample
j. Liquid seal
m. 3-way valve
n. 3-way valve for vacuum pump, oxygen or air.
p. Enclosing chamber

proper mixing. During the preparation of the mixtures a ground glass disc and a mercury seal covered the bottom of the tube. This disc and seal were removed just before attempting ignition. The ignition source was a spark gap ¼ in. long, located 3 in. from the bottom of the tube. The sparking was produced by a General Electric ignition transformer, 250 volt-amperes, 10,000 volts secondary.

Tests were conducted at elevated temperatures to determine the upper limit, and at both elevated and room temperatures to determine the lower limit. This work was performed over a period of six weeks and has been grouped into five series of tests.

Preliminary Tests

The object was to check experimental procedures while determining the lower flammability limit of a liquid composed of 68.3 per cent Fluothane and 31.7 per cent ether (by volume), when vaporized in oxygen. It was also desired to determine, in particular, the effect of doing the tests at room temperature.

TABLE I

RESULTS, SERIES 1

Test no.	Pressure (mm. Hg)	Temp. (°F.)	Pump cycles	Percentage mixture	Flame propagation	Remarks
1	761.5	80	20	11.1	Yes	Loud noise
2	761.5	78	None	10.0	No	
3	761.5	80	None	9.7	No	
4	761.5	80	None	10.5	Partial	1/3 up tube
5	761.0	80	20	10.5	Yes	Loud noise
6	759.5	79	20	10.0	Yes	Loud noise
7	759.0	79	20	9.0	Yes	Loud noise
8	759.0	79	20	7.0	No	
9	759.0	79	20	7.6	Yes	
10	753.0	79	20	7.3	No	
11	753.0	80	20	7.4	Yes	
12	752.0	79	7	7.5	Partial	3/4 up tube

One of the first observations as a result of these tests was that proper mixing was necessary. The lack of propagation or the partial propagation of flame in tests 2, 3, 4, and 12 is attributed to poor mixing.

Another important observation was that pressure increased above atmospheric in the system as the pumping cycles proceeded. This pressure increase was in the order of 30 mm. Hg. An infrared spectral examination was carried out which indicated that no chemical reaction had taken place. It was therefore concluded that the increase of pressure was due to re-evaporation of a small amount of the anaesthetic vapour which had condensed as the oxygen was added to the system. This resulted in a little too much oxygen, but the error was largely compensated for by the fact that the mercury tube for measuring the degree of vacuum had not been tapped after evacuating the system. It was found that tapping the tube resulted in the mercury shifting, usually about an additional 2 mm.

As a result of the observations made during these preliminary tests a more accurate procedure was established for subsequent tests carried out at room temperature. When the oxygen was admitted it was shut off before the pressure in the system reached atmospheric, usually at about 75 mm. Hg of vacuum. After the small amount of condensed vapour had evaporated again, the oxygen necessary to bring the system to atmospheric pressure was added.

In tests at elevated temperature this procedure was not necessary as no condensation occurred.

Lower Limit Tests in Oxygen at Room Temperature

TABLE II

RESULTS, SERIES 2: ANAESTHETIC—68.3% FLUOTHANE AND 31.7% ETHER, BY VOLUME

Test no.	Pressure (mm. Hg)	Temp. (°F.)	Pump cycles	Percentage mixture	Flame propagation	Remarks
13	762.5	76	20	7.35	No	
14	747.0	80	20	7.65	No	
15	741.0	80	30	7.8	Yes	
16	741.0	79	25	7.7	No	
20	759.5	79	25	7.7	Yes	
21	757.0	79	25	7.55	Yes	
22	766.0	78	25	7.41	Yes	Tube black
23	765.5	79	25	7.32	Yes	Tube black
24	765.0	78	25	7.3	Yes	Tube black
25	763.5	80	25	7.2	No	Tube black
26	763.5	80	25	7.2	No	Tube black

Tests 17, 18, and 19 were conducted at elevated temperatures and comprise Series 3.

It is considered possible that differences in barometric pressure may have some effect on the lower limit and may account for there being no propagation of flame in tests 14 and 16. If this is so, it would appear that higher barometric pressures tend to produce a lower limit.

Tests 22 to 26 were carried out after tests to determine the upper flammability limit, during which heavy black smoke was produced when flame propagation occurred. This accounts for the remark that the tube was black in tests 22 to 26. It is believed that if this darkening of the glass surface had any effect it would be to lower slightly the lower limit.

Lower Limit Tests in Oxygen at Elevated Temperature

TABLE III

RESULTS, SERIES 3: ANAESTHETIC—68.3% FLUOTHANE AND 31.7% ETHER, BY VOLUME

Test no.	Pressure (mm. Hg)	Temp. (°F.)	Pump cycles	Percentage mixture	Flame propagation
17	762.0	131	25	7.48	Yes
18	762.0	131	25	7.35	No
19	762.0	131	25	7.4	Yes

Upper Limit Tests in Oxygen at Elevated Temperature

TABLE IV

RESULTS, SERIES 4: ANAESTHETIC—68.3% FLUOTHANE AND 31.7% ETHER, BY VOLUME

Test no.	Pressure, (mm. Hg)	Temp. range, (°F.)	Pump cycles	Percentage mixture	Flame propagation
1	748.0	156 to 160	25	67.3	No
2	746.0	176 to 165	25	53.0	Yes
3	748.5	167 to 161	25	60.0	Yes
4	761.5	156 to 171	25	64.0	Yes
5	762.0	149 to 173	25	66.8	Yes
6	764.0	158 to 194	25	68.0	No

Flammability Tests in Air

A preliminary test was made which consisted of boiling 10 ml. of the anaesthetic in a glass beaker 2 in. in diameter. Matches were lighted and held in various positions in the vapour and it would not catch fire. There was a very small space, in which position the match flame increased a little in size and at the same time a black smoke was produced.

TABLE V

RESULTS, SERIES 5: ANAESTHETIC—68.3% FLUOTHANE AND 31.7% ETHER, BY VOLUME

Test no.	Pressure (mm. Hg)	Temp. (°F.)	Pump cycles	Percentage mixture	Flame propagation	Approximate flame length (in.)
1	763.0	72	30	7.1	No	0
2	760.0	75	30	9.75	No	$\frac{1}{4}$
3	756.0	79	30	11.0	No	$1\frac{1}{2}$
4	763.0	77	27	11.4	No	$\frac{1}{2}$
5	763.0	80	40	12.0	No	2
6	764.0	79	60	15.0	No	3
7	763.0	79	50	20.0	No	3 or 4
8*	754.5	80	20	33.0	No	$\frac{1}{2}$
9	767.5	140 to 149	30	18.0	No	2
10	769.0	140 to 167	25	23.3	No	1

*Test 8 was for a saturated mixture at room temperature.

CONCLUSIONS

The lowest percentage mixtures with oxygen which propagated flame for the three series of tests concerned with the lower flammability limit were 7.4, 7.3, and 7.4, and the lower limit was chosen as the average between the lowest percentage which propagated flame and the next lowest which did not. This resulted in a lower limit in oxygen of 7.25 per cent. Similarly the upper limit in oxygen was 67 per cent.

From the results of the tests with the anaesthetic and air, it was concluded that there is unlikely to be a percentage mixture which will propagate flame in air and that for practical purposes the azeotropic mixture can be considered non-flammable in air.

Summary

Five series of tests—four in oxygen and one in air—were made with an azeotropic mixture received from the University Hospital, University of Saskatchewan, Saskatoon. This sample was labelled 68.3 per cent. Fluothane and 31.7 per cent ether by volume. Flame propagation was upward in a glass tube 2 in. in diameter and 5 ft. long, open at the bottom. The ignition source was the spark produced by a 250 va. General Electric ignition transformer, 10,000 volts secondary. All the tests to determine the upper limit of flammability in oxygen were at elevated temperatures and some of the tests to determine the lower limit were at elevated temperatures. The results in oxygen were *lower limit*, 7.25 per cent; *upper limit* 67.0 per cent. Tests indicated that the azeotropic mixture vaporized in air will not propagate flames and that the liquid has no flash point.

Acknowledgments

Helpful discussions were had with Dr. D. S. Montgomery and Mr. R. G. Draper, senior scientific officers of the Fuels and Mining Practice Division. Miss Frances E. Goodspeed, also of the Fuels and Mining Practice Division, made the infrared spectral examinations.

Résumé

Nous avons fait cinq séries d'expériences—quatre avec de l'oxygène et une avec de l'air—avec un mélange azéotropique reçu de l'hôpital universitaire, Université de Saskatchewan, Saskatoon. Cet échantillon était étiqueté 68.3% de Fluothane et 31.7% d'éther en volume. La propagation de la flamme se faisait de bas en haut à travers un tube de verre de deux pouces de diamètre et de cinq pieds de long; le tube était ouvert à son extrémité inférieure. La source d'allumage était une étincelle produite par un transformateur General Electrique de 250 watts et 10,000 volts. Toutes les expériences pour préciser la limite supérieure d'inflammabilité dans l'oxygène se faisaient à des températures élevées et quelques-unes des expériences pour préciser la limite inférieure étaient également pratiquées à des températures élevées. Voici les résultats dans l'oxygène: *limite inférieure*, 7.25%; *limite supérieure*, 67.0%. Ces expériences nous permettent d'affirmer que le mélange azeotropique vaporisé dans l'air n'entretient pas les flammes que le liquide n'a pas de point d'explosion.

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HALOTHANE-INDUCED HYPOTENSION AND THE EFFECT OF VASOPRESSORS

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EPINEPHRINE, norepinephrine, ephedrine, and desoxyephedrine have been reported to have initiated ventricular arrhythmias in dogs anaesthetized with halothane (1). On the other hand, no irregularities other than bradycardia were found under similar conditions with methoxamine and phenylephrine (1, 2). Cardiac irregularities occuring with epinephrine and norepinephrine administrations in patients under halothane anaesthesia are well documented (3–5). Brindle *et al.* (4) reported safely using methoxamine and phenylephrine infusion for hypotension during halothane administration. Other authors have reported (5, 6) successfully administering methoxamine for sudden acute hypotension during halothane anaesthesia. Wyant and his co-workers (7) gave doses of 2.5 mg. of phenylephrine intravenously to hypotensive subjects receiving halothane and found premature ventricular contractions in two of four patients.

This study was undertaken to determine the effects of methoxamine, phenylephrine, and mephentermine given intravenously during extreme hypotension induced by halothane.

METHOD

Seventy studies on 48 mongrel dogs weighing from 8 to 20 kg. were analysed for this series. Dogs that were used for a second study had a three-day rest between experiments. The animals were given sufficient thiopental to allow endotracheal intubation and vessel canulations. The animals were respired throughout the experiment with a volume-limited ventilator (Palmer Ideal Pump) with a 30 per cent oxygen and a 70 per cent nitrogen mixture. Tidal volumes were adjusted to maintain end-tidal carbon dioxide tensions of 35–40 mm. of mercury at the beginning of each experiment. The dogs were allowed to awaken after the induction dose of thiopental before halothane was started. Halothane vaporized with a "bubble through vaporizer" was given in a semi-closed system with carbon dioxide absorption in concentrations necessary to lower the intra-aortic pressure to 20–40 mm. of mercury within a 3–5 min. period. When the desired hypotension was achieved, the anaesthetic was discontinued and the ventilator adjusted to deliver twice the pre-existing tidal volume. Eight of the dogs in the series were not given vasopressors and are designated as controls. All other animals received vasopressors when the blood pressure decreased to the desired hypotensive level. Vasopressors were diluted with saline and 1 ml. of this dilution was given every 30 sec. until a pressor response was initiated after which it was discontinued (phenylephrine .5 mg./ml., mephentermine 5 mg./ml.;

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methoxamine 2 mg./ml.). Cardiac rhythm was recorded with a Sanborn electrocardiograph (lead II) and blood pressure measured with a mercury manometer through an intra-aortic catheter.

Results

Seven of the eight dogs serving as controls who were rendered hypotensive with halothane and hyperventilated after discontinuance of the anaesthetic returned to "normal" blood pressures within a 10 min. period. The remaining animal developed cardiac standstill. Most of the animals under halothane exhibited ECG changes of depression or inversion of T waves and bradycardia. No significant cardiac arrhythmias occurred as the blood pressure fell or as it returned toward normal.

A high incidence of cardiac irregularities including ventricular fibrillation followed the administration of vasopressors. In Table I are presented the irregularities seen both in the controls and in those receiving vasopressors. Each animal studied is listed only once and is listed under the most severe arrhythmia noted. Many animals developed more than one type of arrhythmia, often having progressive patterns of ventricular extrasystoles, multifocal ventricular rhythm, paroxsymal ventricular tachycardia, and ventricular tachycardia. Atrioventricular block occurred in four out of twelve animals receiving methoxamine. Total doses of vasopressor given before a rise in blood pressure was initiated showed wide variations: methoxamine 2–12 mg.; phenylephrine 0.5–5 mg.; and mephentermine 5–45 mg. No correlation could be found when the dose of drug on a mg./kg. basis was compared with severity of irregularities (Fig. 1). When the data were subjected to the chi-square test, no significant differences were found between the incidence of irregularities between the groups receiving phenylephrine, methoxamine, or mephentermine.

To determine if hyperventilation following hypotension influenced the incidence of irregularities with vasopressor administration, eight dogs were picked at random during the course of the study and were maintained at control tidal volumes. There appeared to be no difference in the incidence or severity of the irregularities between those animals treated in the above manner and the other animals receiving vasopressors in the study.

Twenty-two dogs were given atropine 1 mg./kg. intravenously and after 15 min. were subjected to halothane anaesthesia to the point of hypotension and then given vasopressor therapy. While the incidence of irregularities was unchanged, none of the animals pretreated with atropine developed ventricular fibrillation (see Table I). This finding, however, namely the reduction in ventricular fibrillation in the dogs receiving atropine when compared with those not receiving atropine, was not found to be significant when the data were subjected to the chi-square-test $p < .250$.

None of the dogs who had a pressor response following the catechol amines exhibited arrhythmias until the mean blood pressure reached 100 mm. of mercury, the average of 43 dogs was 140 mm. of mercury with a range of 100 to 220 mm. of mercury. Attempts to titrate vasopressors to prevent rises over pre-existing blood pressures were largely unsuccessful. Two dogs did not develop hypertension

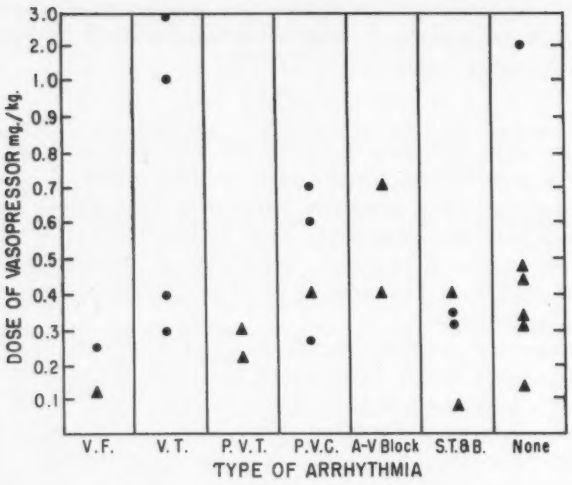

FIGURE 1. Variations in dosage of vasopressor necessary to correct hypotension and the most severe irregularity occurring with the doses of methoxamine and mephentermine used.

V.F., ventricular fibrillation; V.T., ventricular tachycardia; P.V.T., paroxysmal ventricular tachycardia; P.V.C., premature ventricular contractions; S.T. & B., sinus tachycardia and bradycardia; closed circle, mephentermine; closed triangle, methoxamine.

and also did not have arrhythmias. However, upon administration of additional vasopressors, hypertension and irregularities were initiated.

Eight dogs (not included in Table I) having cardiac arrhythmias following vasopressor therapy for halothane-induced hypotension were treated with intravenous trimethaphan camphorosulfonate (Arfonad). Concomitant with a fall in blood pressure from the hypertensive state cardiac irregularities ceased and the ECG pattern returned to normal sinus rhythm.

COMMENT

No attempt was made to determine the cause of the cardiac arrhythmias and we cannot conclude from results of this study that halothane *per se* "sensitized" the myocardium to the catechol amines. Other factors which may have influenced development of irregularities were: (i) hypotension during the halothane administration with presumably some degree of tissue hypoxia and hypercarbia: (ii) hypertension following administration of vasopressor. Lurie and co-workers (8) found that hypercarbia induced cardiac irregularities in subjects anaesthetized with cyclopropane. Indeed, the authors have observed arrhythmias in some dogs under barbiturate anaesthesia with each of the sympathomimetic amines used in this study but only when hypertension was produced. Stutzman *et al.* giving

TABLE I

INCIDENCE OF ARRHYTHMIA FOLLOWING VASOPRESSOR ADMINISTRATION DURING HYPOTENSION INDUCED BY HALOTHANE*

Type of arrhythmia	No vasopressor	Phenylephrine Atropine (1 mg./kg.)		Mephentermine Atropine (1 mg./kg.)		Methoxamine Atropine (1 mg./kg.)	
Ventricular fibrillation (hypotensive)		2				1	
			(.1 mg./kg.)				
Ventricular fibrillation (hypertensive)		2	1	1		1	
Cardiac standstill	1	2					
Ventricular tachycardia		4	4	2	2		
Paroxysmal ventricular tachycardia			1				2
Premature ventricular contractions		1					
Multifocal venticular rhythm				1		1	1
Bigeminal rhythm			2				
Occasional extrasystoles			1	1	3		
Atrioventricular block		1		1		4	
Sinus arrhythmia				1			
Sinus bradycardia		1				5	
No arrhythmias	7		2	1			2
Ventricular arrhythmias (%)	12	92	81	75	100	58	60

*Each dog is listed under the most severe irregularity which occurred.

unanaesthetized dogs 1 mg./kg. of methoxamine found a 30 per cent incidence of atrioventricular block (9). Brofman and co-workers (10) state that mephentermine in "unusually large doses" causes premature ventricular contractions in dogs under pentobarbital anaesthesia. The association of cardiac irregularities with hypertension following sympathomimetic amines has also been described by others. Raventos (2) using dogs anaesthetized with halothane concluded that ventricular arrhythmias had a relationship to elevation of blood pressure because equipressor doses of norepinephrine and epinephrine were equally active in producing arrhythmias. On the other hand, he states that mephentermine and methoxamine produce rises in blood pressure comparable to those with epinephrine without inducing arrhythmias. Moe *et al.* (11) using dogs anaesthetized with cyclopropane found that when a rise in blood pressure after epinephrine was prevented by means of a "pressor regulator" the incidence of irregularities diminished and the animals could tolerate higher doses of epinephrine before arrhythmias occurred. Cummings and Hays (12), on the other hand, could find no definite correlation between the capacity of adrenergic drugs to elevate blood pressure and induce cardiac irregularities in dogs under cyclopropane anaesthesia. Furthermore, the above authors state that isopropylnorepinephrine (Isuprel) induces cardiac arrhythmias during hypotension produced by the drug. Ventricular fibrillation following administration of phenylephrine, methoxamine, or mephentermine to our knowledge has not been reported by others nor has it been observed by us in unanaesthetized dogs or those under barbiturate anaesthesia.

Nickerson *et al.* (13) found that atropine in large doses 1 mg./kg. gave partial

protection to dogs against epinephrine-induced arrhythmias with cyclopropane. It was concluded that atropine had its major protective action by some direct effect on the myocardium. Levy (14) reached a similar conclusion using chloroform anaesthesia. It should be emphasized, however, that the dose of atropine used in the above studies and in this present study is 50 to 100 times as great on a weight basis as that usually employed clinically to produce parasympathetic blockade.

We have not as yet determined the cause for the cessation of arrhythmias after trimethaphan camphorosulfonate administration. Possible explanations are that it may be the result of a peripheral action of the drug reducing blood pressure, a direct myocardial action, or of ganglionic blockade.

Summary

Seven of eight dogs on fixed-volume ventilation and subjected to concentrations of halothane which lowered blood pressure to 20–40 mm. of mercury recovered when the anaesthetic was discontinued and hyperventilation was instituted. None of the dogs developed arrhythmias while hypotension was being induced or as its blood pressure returned to pre-existing levels. The remaining animal developed cardiac standstill.

Phenylephrine, methoxamine, and mephentermine administration during hypotension was followed by a high incidence of cardiac irregularities.

Pretreatment of dogs with 1 mg./kg. of atropine did not prevent arrhythmias.

Trimethaphan camphorosulfonate (Arfonad) given at the time irregularities occurred produced a fall in blood pressure with a concomitant conversion of the ECG pattern to normal sinus rhythm.

Acknowledgments

We wish to thank Dr. George Carman of the Division of Cardiovascular Medicine of the University of Utah for his assistance with electrocardiograph interpretations.

Résumé

Sur huit chiens dont la ventilation était maintenue à un volume fixe et qui étaient soumis à des concentrations d'halothane suffisantes pour abaisser leur tension artérielle de 20 à 40 mm. de Hg, sept ont récupéré à la cessation de l'anesthésie et à l'installation d'une hyperventilation. Aucun des animaux n'a présenté d'arythmie au cours de l'hypotension pas plus qu'au retour de la pression à la normale. Le huitième chien a présenté un arrêt cardiaque en diastole. Au cours de l'hypotension, l'injection de phenylephrine, de methoxamine et de mephentermine a entraîné de très fréquentes irrégularités cardiaques. Le traitement préventif de ces arythmies en injectant 1 mg./kg. d'atropine n'a pas été efficace. Injecté au moment de l'apparition des irrégularités, le trimethaphan camphorosulfonate (Arfonad) a provoqué une chute de pression et une modification concomittante du tracé électrocardiographique en un rythme sinusal normal.

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VASOPRESSORS[1]

P. R. BROMAGE, M.B., B.S., D.A., F.F.A.R.C.S.[2]

WHEN a man travels in dangerous country, he carries a gun and if he is wise he knows what his gun will do in terms of range, stopping power, and speed of action. We often turn to vasopressors as a weapon to get our patients and ourselves out of difficult situations, but unfortunately we do not always have a very clear idea of what these drugs can do, and we sometimes find ourselves in the embarrassing situation of trying to stop an elephant with a shotgun, or worse still we may be overanxious and trigger-happy, and our foolishness may stir up trouble amongst the natives who might otherwise have been peaceably disposed towards us.

But before we turn to violent methods of self-protection against the dangers of hypotension we must make sure that gentler ways may not be better. Perhaps we should feed the prowling enemy, and win him over by replete contentment. If the circulation is half empty, we will continue to deal with a dangerous situation until it is filled and appeased. One often sees anaesthetists using vasopressor drugs to treat hypovolaemic hypotension when their time would be better spent restoring a depleted blood volume.

Let us consider the blood pressure in terms of blood volume and distension of the vascular bed, without the complicating factor of cardiac output. Imagine that the heart is momentarily arrested, and the pressure throughout the circulatory system can be measured simultaneously. This has been done experimentally in dogs by Guyton and his colleagues (1). The pressure obtained under these circumstances is called "the static blood pressure," or "mean circulatory filling pressure." This pressure is the basic background pressure on which the pumping action of the heart is superimposed. Figure 1 is constructed from Guyton's data, and shows the relationship between the blood volume, and the static blood pressure, and the tone of the blood vessel walls.

Normally the static blood pressure is about 6–8 cm. H_2O. If the blood volume is reduced by haemorrhage or dehydration, the static filling pressure also falls until it reaches zero. This point is reached after losing about 40 per cent of the blood volume, and at this point the animal dies, for no matter how hard the heart pumps there is just not enough fluid to fill the whole vascular system. Beyond this point vasodilatation and vasoconstriction have no meaning, for their pressure-volume (or compliance) curves have all reached zero.

However, at points between the normal blood volume and the "bled-out volume" vasoconstriction may be very important, and at extremes of low blood volume it may make all the difference between life and death. For example,

[1]Paper read at a meeting of the Quebec Division of the Canadian Anaesthetists' Society, February 6, 1960.

[2]Department of Anaesthesia, Royal Victoria Hospital, Montreal, P.Q.

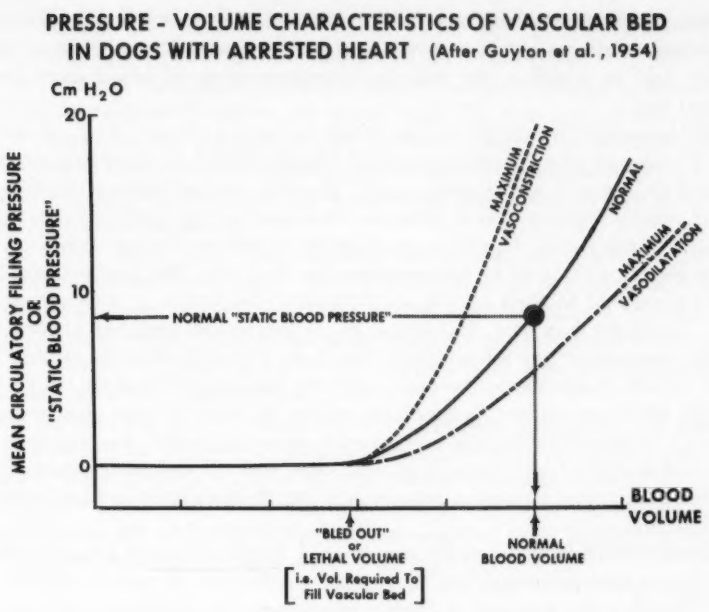

FIGURE 1

prolonged bed-rest in itself reduces the blood volume (2) and many bed-ridden patients live happily with only about two-thirds of the normal amount of blood in their bodies, but they have constricted large areas of their vascular bed to make up for the loss of volume. Now, if we take such a patient and suddenly remove his vasoconstriction by means of a high spinal blockade or by deep general anaesthesia, we will precipitate his "static blood pressure" from a fairly useful level to one which is almost lethally low, and death may occur from acute hypotension and coronary ischaemia. On the other hand, a patient with a large blood volume and vasodilatation (as in pregnancy) may be living on the bottom line, labelled "Vasodilatation" in Figure 1. If we exhibit a vasoconstrictor here the "static blood pressure" may rise to alarming heights with signs of left ventricular failure and encephalopathy.

Therefore when we think of vasopressors, we should think of them applied to the broad background of blood volume and "static filling pressure," and in this way we shall be spared many disappointments and embarrassing moments.

Let me give an actual example. A 200 lb. woman with hypertension and chronic bronchitis was to have a pelvic repair under spinal analgesia. In the hospital concerned it was the practice to give a vasopressor drug before spinal blocks, and the patient was given 50 mg. ephedrine subcutaneously. The spinal was administered and a few minutes later she was placed in the lithotomy position. The block only extended to T_{10} and everyone was amazed when the patient suddenly convulsed and showed all the signs of a cerebrovascular accident.

In effect, it would have been surprising if she had not had one, for she was already hypertensive and yet she was given a powerful pressor drug when it was not needed, and in addition she had an autotransfusion of blood from her own elevated legs.

Now, supposing we decide we are likely to need a pressor drug, what are we going to use and why? Most of us would answer: "Well, I use so-and-so, because I'm used to it, and it works pretty well." We may even advance scientific reasons for our choice, arguing that it either is, or is not, a drug which affects the force and pace of the heart, depending on whether or not we favour such a property. In the genealogical tree of vasopressors, we find that the families are divided mostly according to their effects on the heart—the inotropic and non-inotropic drugs. The body has been diplomatic in its patronage, and has chosen for its natural vasopressor one which has a foot in both camps: that is, noradrenaline, which is both vasoconstrictive and positively inotropic. When we try to correct a faulty pressure system, perhaps we might be wise to plan our vasopressor campaign in terms of what the body would choose if it could, keeping noradrenaline prominently in our minds. I do not mean that we should use noradrenaline infusions every time we need a vasopressor, but that it should not be too far from our thoughts.

Professor Burn and his colleagues in the Department of Pharmacology at Oxford have done much to place vasopressor medication on more rational grounds (3–6). Figure 2 is a synopsis of Burn's hypothesis. He postulates that all nerves (post-ganglionic as well as pre-ganglionic) are cholinergic. The post-ganglionic nerves secrete acetylcholine, which in turn releases noradrenaline from depots close to the effector organ (that is, the smooth muscle of the vessel walls).

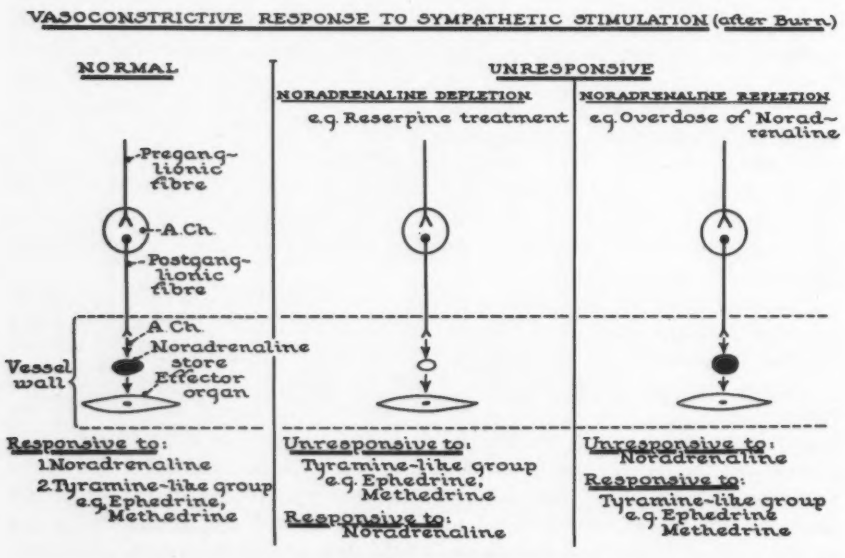

FIGURE 2

Under normal circumstances the noradrenaline depots are responsive to all sorts of pressor agents, both noradrenaline itself and that group of pressor agents which are indirect vasopressors, that is, which act by releasing noradrenaline. Now, if the noradrenaline depots are empty (as in the reserpine-treated patient), then the indirect stimulators no longer work since there is no noradrenaline for them to release. Under these circumstances methedrine and ephedrine are useless, but, oddly enough, the effector organ is extremely responsive to very small doses of circulating noradrenaline.

On the other hand, when the noradrenaline stores are overfilled (as after prolonged noradrenaline infusion), they show signs of constipation, and cannot evacuate themselves without aid. Under these circumstances a noradrenaline liberator, such as methedrine, is the drug of choice and members of this group should be considered when a noradrenaline drip fails to raise the blood pressure.

Two cases serve to illustrate this point.

Figure 3 shows the blood pressure chart of a patient undergoing an operation for splenorenal shunt under continuous epidural blockade. Notice the very small amounts of noradrenaline required to raise the blood pressure. 1–2 μg./min. is all that is required (that is 10–20 drops per minute of a solution containing 0.5 mg. noradrenaline in 500 ml.). This is the right strength of noradrenaline to use, but it is one-quarter of that recommended by the makers.

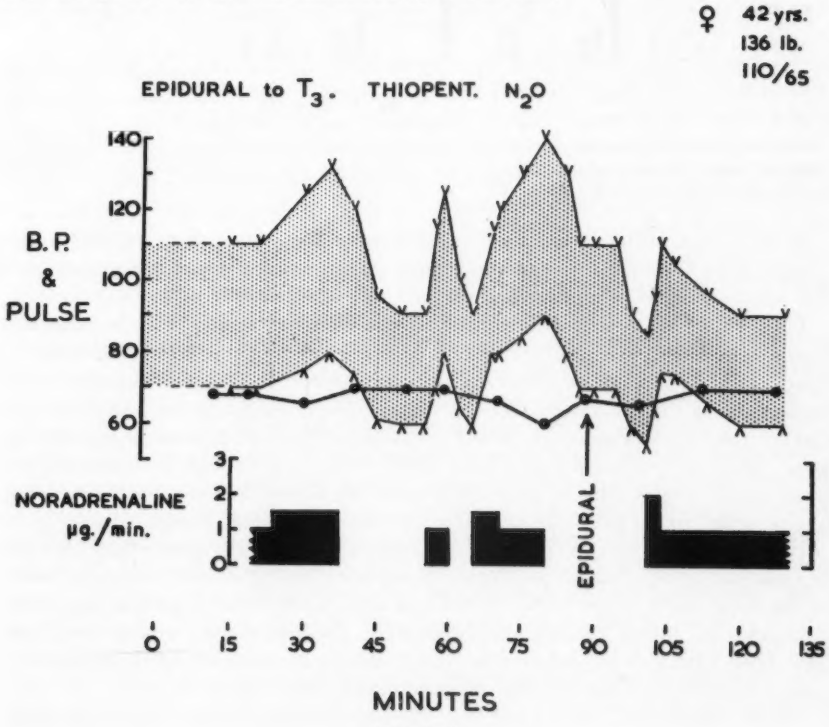

FIGURE 3

Figure 4 shows the blood pressure chart of a patient having a phaeochromocytoma removed. After excision of the tumour he was unresponsive to enormous amounts of infused noradrenaline. At point M, 10 mg. methedrine were injected intravenously. This enabled him to release his own noradrenaline stores, and he maintained a good blood pressure thereafter.

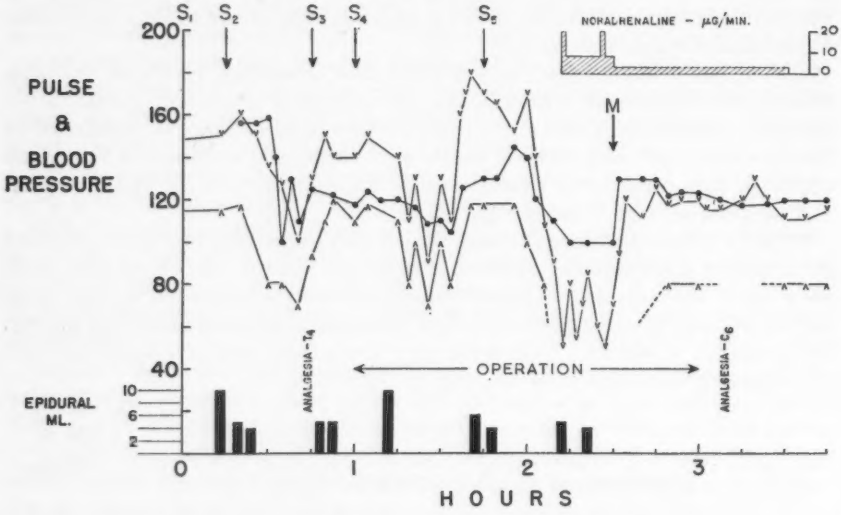

FIGURE 4. Blood pressure chart of 8-year-old boy undergoing excision of phaeochromocytoma Epidural using 1.5 per cent Xylocaine. 10 mg. methedrine injected intravenously at M. Blood samples (for catecholamines) taken at S_1–S_5.

In this brief outline I want to confine most of my remarks to the effects of vasopressors on the peripheral resistance, but in passing I will just touch on a few points concerning the cardiac output.

Pulse rate has an important effect on the cardiac output; so in hypotensive states associated with bradycardia we should turn to drugs which increase the heart rate rather than those which slow it. Atropine by itself is a useful vasopressor under these circumstances; 1/300–1/150 gr. will raise the pulse rate and elevate the blood pressure by about 15–20 mm. Hg. Consciousness may do the same thing, as we can see in Figure 5 (7). Here is a patient with an epidural block to T_7. Under light nitrous oxide sleep the blood pressure fell 35 mm. Hg, but returned to the previous level immediately the patient awoke.

Hydrocortisone and calcium are two other important drugs which should not be forgotten in our concern for the blood pressure. Since they are not vasopressors in the strict sense of the word, we will not dwell on them, but we may find them indispensable under certain circumstances: hydrocortisone, where corticoids have been administered before operation; calcium in states where the circulating ionisable calcium is low, as after massive blood transfusion.

Finally, we turn to what I call the Therapy of Desperation—the use of vasopressors when we cannot think of anything else to do, as in such conditions as

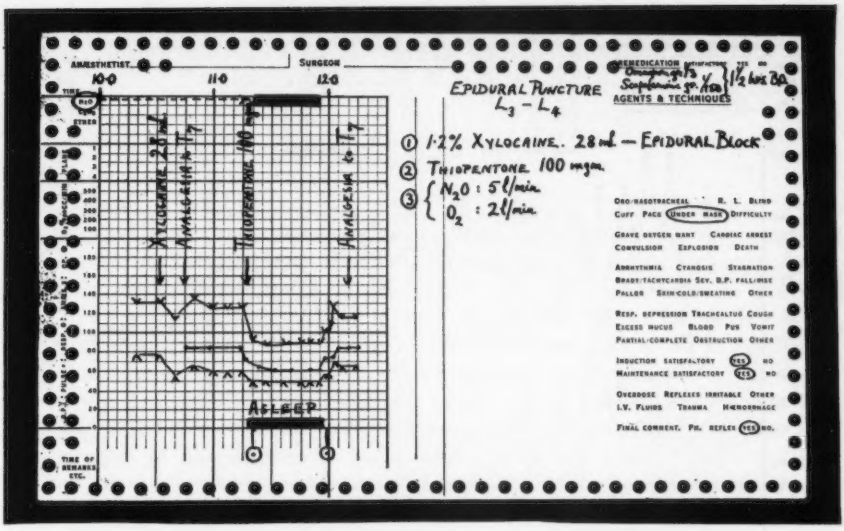

FIGURE 5. Effect of consciousness on blood pressure.

coronary thrombosis and other forms of intractable hypotension. Figure 6 shows the blood pressure chart of a girl who had some infected blood given to her during a spinal fusion. Toxaemia followed, accompanied by severe hypotension which was resistant to methedrine, hydrocortisone, noradrenaline, and phenylephrine. However, she had the resilience of youth, and she felt better with her hypotension than she did with the enormous doses of vasopressors which were poured into her; so her blood pressure was suffered to remain low. In the fulness of time the fever left her, and then, and then only, did she become normally responsive to reasonable doses of vasopressors, but by this time, of course, there was no point in using them.

When faced with this type of case we are sorely tempted to use poisonous doses of pressor drugs. We are tempted because we are ignorant and know no better, and it seems the only thing left in our power to do—apart from leaving things to Nature. But we are not always very good at doing that.

My view on vasopressors can be summed up quite briefly. Employ them as you would a lawyer—that is, do not use one unless you have to, and if one *does* have to, choose the best you can get. If you decide to follow Nature's example and use noradrenaline, use it with the same moderation that the body does. Recent work has shown this to be about 2–3 μg./min. (8). This is 20–30 drops per minute of a solution containing ½ ml. noradrenaline solution in a 500 ml. bottle, and this is more than you need to keep the blood pressure at normal levels after a total spinal blockade.

If the noradrenaline stores have become overfilled and constipated after prolonged noradrenaline overdosage, we must use a cathartic or noradrenaline releaser, such as methedrine.

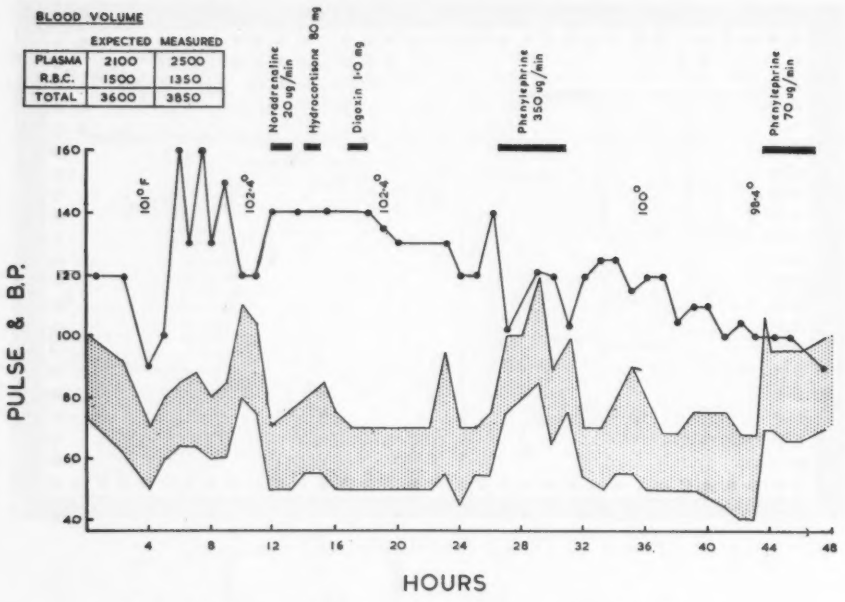

FIGURE 6. Toxaemic hypotension refractory to vasoconstrictor drugs.

Under normal circumstances we can be lazy and use other and longer-lasting pressor drugs if we wish, but when the noradrenaline stores are depleted, or when we want quick and certain action, we should turn to noradrenaline as the bulwark of our defence.

In toxaemia and central cardiac failure our knowledge is still incomplete, but at present it seems that vasoconstrictors are not likely to do much good.

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THE EFFECTS OF ANAESTHETIC AGENTS ON THE CARDIOVASCULAR SYSTEM: A REVIEW[1]

ALLEN B. DOBKIN, M.D.

IN WILLIAM HARVEY'S[2] GREAT WORK, *De motu cordis* (1628), we may read how he was led to his conclusions about the circulation of the blood by *exact observations*, *exact experiments*, and *exact thought* (1). The 300 years since his time have brought forth new techniques and new devices for the investigation of the circulation and heart function (2–8). However, there is still no substitute for the three great components of Harvey's method if the anaesthetist wishes to determine how anaesthetics affect the heart, for we still do not have a clear picture of the many factors involved in normal heart function and how these are affected by stress, disease, and anaesthesia (9, 10, 11).

The key role of the heart is that of a *unidirectional pump*. This pump supplies the motive force of venous blood to the lungs and of arterial blood to the systemic channels which perfuse the vital organs. The brain receives 750 ml./min., which activates nervous functions. The kidney receives 1500 ml./min., which regulates disposal of waste. The liver receives 1500 ml./min., which regulates many of the chemical reactions in the body. The heart muscle itself requires 200 ml./min. These four vital organs normally receive 80 per cent of the total blood flow.

The ideal measurement of heart function would be its power, or work per unit of time. However, we can only measure with ease the resistances which the heart must overcome to force the blood into the various regions of the body. These resistances consist mainly of: (*a*) the viscosity of the blood which affects blood flow; (*b*) the distensibility of blood vessels which affects peripheral resistance; (*c*) the inertia of the blood which affects myocardial contractility. And these three are related thus:

$$\text{Peripheral resistance} = \frac{\text{Mean arterial blood pressure}}{\text{Blood flow/unit time}}$$

These resistances constitute the venous and arterial blood pressure. This is the pressure (measured in mm. Hg) exerted by the blood on the walls of the vessels in which it is flowing.

(*a*) The *viscosity of the blood* or its internal friction varies with the haematocrit. It takes approximately five times the force (dynes/cm./sec.) to move a volume of blood in a tube a certain distance as to move water the same distance. The major part of the heart's energy is required to overcome viscous resistance. *Remember*: haematocrit increases during anaesthesia; plasma volume falls and red cell volume increases (relatively).

[1]From the Department of Anaesthesia, University of Saskatchewan College of Medicine and University Hospital, Saskatoon.

[2]Born April, 1578; died June, 1657.

(*b*) *Distensibility of the vessels* is the relation between changing volume and changing pressure, and is somewhat analogous to the compliance of the lung. There is a tremendous difference between the distensibility of the veins and the distensibility of the arteries. In the dog, there are approximately 700 ml. of blood on the venous side of the circulation at a mean pressure of 7 mm. Hg, whereas on the arterial side there are about 200 ml. at a mean pressure of 100 mm. Hg. The veins can alter their distensibility tremendously, whereas the arteries can only change by a multiple of 4.

This difference is clinically significant when one considers that the vascular volume changes with blood loss. As haemorrhage progresses, distensibility is reduced progressively in the veins and arteries. This reduction in vascular volume is induced by the sympathetic nervous system and circulating catechol amines, and compensates for reduced blood volume enough to maintain an adequate blood flow. When irreversible shock begins, distensibility increases—especially on the venous side. Thus, a very large volume of blood can be injected without clinical response because the blood may merely distend the veins and will not reach the "pump."

Remember: as anaesthesia deepens, we always see increasing *distension of the veins* due to loss of peripheral venous tone. This eventually reduces the return of blood to the heart.

(*c*) *Inertia of the blood* means the persistence of the blood in its state of rest, or uniform motion that requires force to accelerate. At the end of cardiac diastole, the blood in the heart exerts an enormous amount of energy in a very short time (.04 sec.) to get this flow started. This powerful thrust is transmitted to the aorta, and can be observed in the recoil of the whole body on the ballisto-cardiograph. *Remember*: as anaesthesia deepens, this cardiac power is progressively reduced.

Another important concept in anaesthesia is the ratio of arterial to venous resistance. This ratio may affect the perfusion pressure in the brain, heart, liver, and kidney, especially during deep anaesthesia, hypothermia, or induced hypotension with ganglion-blocking drugs. When the arterial resistance is increased, the arterial pressure rises without significant change in the cardiac output, whereas increasing the venous resistance causes both the arterial pressure and the cardiac output to fall drastically. On the other hand, a proportionate increase in both the arterial and the venous resistance does not lower the blood pressure, but the cardiac output is depressed moderately.

When the blood vessel walls are normal, pre-arteriolar resistance is responsible for 5–15 per cent of aortic pressure. During haemorrhage and deep anaesthesia, pre-arteriolar resistance rises and may be responsible for 50 per cent of the aortic pressure. Under these circumstances, the heart uses up half its energy in getting blood to the arterioles. Tissue perfusion is then reduced considerably.

Specific Effects of Anaesthetics on the Heart

It is difficult to state the relative safety of any anaesthetic agent with respect to its action on the heart, because this safety depends more on the skill with

which each drug is administered, and on the therapeutic measures that the wise anaesthetist employs, than on the inherent properties of any anaesthetic drug.

The cardiovascular effect of each agent depends mainly on the route, rate, and concentration of its administration; on whether the patient is allowed to breathe spontaneously or by augmented ventilation; on the depth and duration of anaesthesia, and on the patient's general physical condition—with primary consideration to his pre-anaesthetic cardiopulmonary function and circulating blood volume.

The effect of anaesthetic agents on haemodynamics is especially difficult to define because the normal circulation always initiates circulatory reflexes and carries endogenous substances secreted in response to the injected poisons. These act on various aspects of circulatory dynamics to prevent over-all change. It is essential, therefore, to record simultaneously as large a number of dependent variables as possible. These variables give a more reliable clue to the major parameters affected and the direction of such change. *It is rarely possible to draw conclusions about the mechanisms of circulatory effects of any drug from the changes it may cause in a single dependent variable such as the cardiac output.* From the haemodynamic point of view, the most important observations that we should make are continuous or intermittent recordings of:

Arterial blood pressure
Venous blood pressure
Heart rate and circulation time
ECG
Response to posturing; atropine, epinephrine, methoxamine and cedilanid
Blood volume (plasma and cells) and venous haematocrit
Arterial oxygen saturation, pH, pCO_2, and oxygen consumption
Cardiac output and stroke volume (dye or rhisa)
Force of myocardial contraction (strain gauge bridge)

Direct measurement of the arterial blood pressure provides the most important single measurement because: (*a*) right ventricular output is ultimately reflected in left ventricular output and the arterial blood pressure—thus indicating venous return; (*b*) over-all circulatory effects are evident promptly; (*c*) instantaneous beat to beat responses can be followed.

There are a few recognized specific effects which each agent exerts on the heart—either directly on its force of contraction and on its excitability, or indirectly through release of endogenous hormones, epinephrine, norepinephrine, acetylcholine, histamine or serotonin; or by changing peripheral venous tone, which affects the return of blood to the heart; or through respiratory depression, which causes myocardial hypoxia and acidosis (Fig. 1).

In general, the depression of respiration by any anaesthetic initially causes an increase in the force of myocardial contraction followed by a progressive decrease. A progressive decrease in myocardial contractility accompanies increasing depth of surgical anaesthesia, regardless of the drug selected. The state of vasoconstriction that is seen before induction of anaesthesia rapidly disappears and peripheral blood flow increases with deepening anaesthesia. This is accompanied by decreased blood flow in the major organs in the body. In the presence of heart disease, all cardiovascular changes caused by anaesthesia are aggravated.

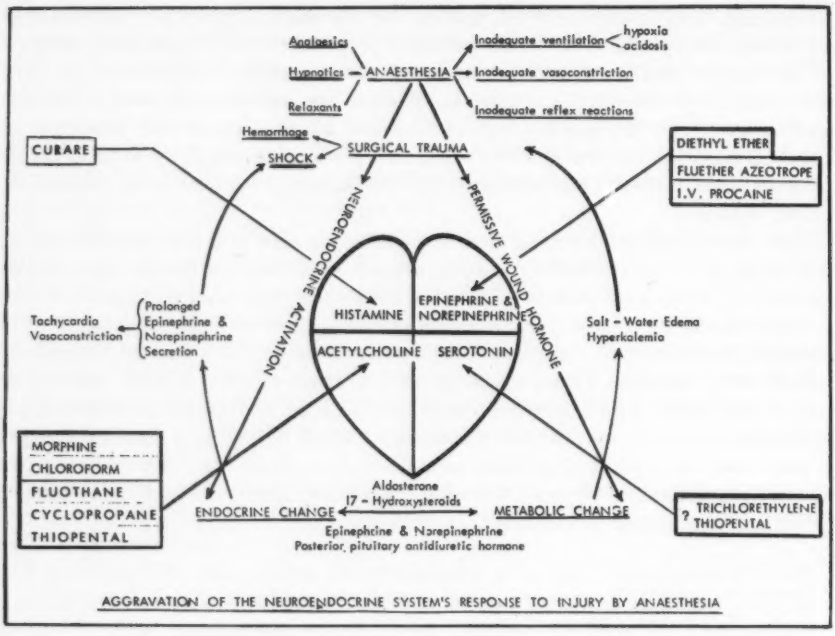

FIGURE 1

SPINAL ANAESTHESIA (12–16)

The effect of spinal anaesthesia on the heart is mainly secondary to changes in peripheral arterial and venous resistance, and in blood flow. In general, the effect varies with the height of the sympathetic block, which paralyses the sympathetic vasoconstrictor fibres at the pre-ganglionic level. The specific changes will be outlined with respect to the effects as seen *without a vasopressor* (Fig. 2).

Sympathetic block at the pre-ganglionic level affects vasomotor tone of the arterioles, which accounts for 60 per cent of the systemic peripherial vascular resistance. The other 40 per cent is maintained by capillary and venous blood flow.

Blood pressure. A fall in arterial blood pressure is the most frequent immediate effect of spinal anaesthesia. Many theories have been offered as to the aetiology: haematogenous intoxication; denervation of adrenal glands; reduced tone of skeletal muscles, venous dilatation, and pooling of blood; direct paralysis of vasomotor and respiratory centres; hypotension—secondary to respiratory insufficiency; and so on.

The hypotension following spinal anaesthesia is mainly the result of paralysis of pre-ganglionic sympathetic fibres which transmit motor impulses to the smooth muscle of the peripheral vessels. The degree of fall in blood pressure is in direct

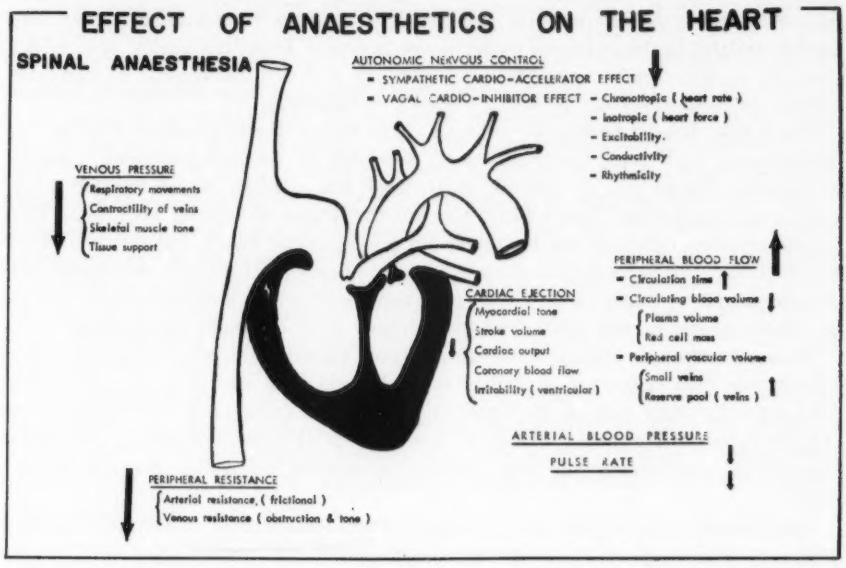

FIGURE 2

proportion to the number of sympathetic fibres blocked. Spinal anaesthesia given after total sympathectomy produces no change in blood pressure.

Clinically, hypotension does not become marked until the sensory block extends above the costal margin. It was believed that this hypotension was due to the splanchnic block, with pooling of blood in the abdominal viscera, but it has been shown clinically and experimentally that there is no excessive pooling in this area.

The mechanism of hypotension due to sympathetic paralysis by spinal anaesthesia is now explained in two ways. First, the generalized arterial and arteriolar dilatation causes a decrease in peripheral vascular resistance, which is great enough to account for the major portion of the hypotension. Secondly, hypotension is secondary also to a decrease in cardiac output, as a result of peripheral pooling and diminution of venous return to the heart.

In some circumstances hypotension may be predominantly due to a decrease in cardiac output; in others it is primarily due to decreased peripheral resistance, or a combination of both. When both fall during spinal anaesthesia, the loss of peripheral resistance precedes the fall in cardiac output. If the posture of the patient augments venous return and cardiac output is maintained, hypotension is related mainly to the fall in peripheral resistance. If vasoconstrictors are administered to maintain peripheral resistance, but hypotension still occurs, then it is due mainly to a fall in cardiac output. Relatively minor degrees of hypotension are mainly the result of changes in peripheral resistance, but if the pressure continues to fall below a critical level, fall in cardiac output is responsible. This can be illustrated when total subarachnoid sympathetic block is given to a normal

patient: systolic blood pressure will fall from 120 to 90 if venous return and cardiac output are maintained by head-low position. If the horizontal or head-up position is then taken, gravitational pooling will reduce venous return and cardiac output, resulting in abrupt severe hypotension.

Pulse rate. Bradycardia may be seen. This varies directly with the height of anaesthesia. It is partly attributed to paralysis of the pre-ganglionic cardiac accelerator fibres (T_{1-4}), leaving control of the cardiac pacemakers to the inhibitory vagal effect. It is related also the the degree of arterial hypotension.

The relation between the height of the sympathetic block and the degree of hypotension is no more precise than the relation between the height of anaesthesia and the degree of bradycardia. Pulse rate and blood pressure changes vary widely in clinical practice even with the same sensory level of spinal anaesthesia.

Pulse rate changes appear to be most closely related to arterial blood pressure alterations, and these are probably related mainly to the changes in venous return to the right side of the heart. Lowering the pressure in the great veins and the right auricle reflexly produces bradycardia (Bainbridge reflex). This may explain the bradycardia that often accompanies even low levels of spinal anaesthesia.

Theoretically the hypotension of spinal anaesthesia should cause tachycardia, reflexly mediated through the pressor-receptors of the carotid sinus and aortic arch. However, the Bainbridge reflex may be dominant over those of the pressor-receptors and the efferent arc of reflexes from T_{1-4} may be blocked by the anaesthesia (afferent arc is parasympathetic in origin and is unaffected).

Cardiac output falls almost invariably with high spinal anaesthesia, but the extent of the fall varies widely among patients. There is a general relation between the height of spinal anaesthesia and the fall in cardiac output, which follows the change in venous return to the heart. The depression of venous return is determined by the extent of the sympathetic paralysis, peripheral vasodilatation, and the posture of the patient. During high blocks, most of the pre-ganglionic sympathetic fibres are paralysed, causing generalized vasodilatation, loss of arteriolar and venous tone, and pooling of a large portion of the total blood volume in the periphery. The extent to which the cardiac output will fall depends on the position of the denervated area with respect to the heart. By having the patient in slight head-down position during high spinal anaesthesia, the decrease in venous return to the heart and in cardiac output is reduced. Head-up tilt, on the other hand, may so diminish the venous return and cardiac output that the heart will stop.

Remember. After spinal anaesthesia has stabilized, the peripheral resistance usually remains constant, and changes in blood pressure are then due to alterations in cardiac output or circulating blood volume. These are corrected by posturing, blood transfusion, or increasing myocardial tone with a vasopressor such as ephedrine. When respiration is very depressed, artificial respiration with intermittent positive pressure may further lower the blood pressure if venous return is not assisted by head-low posture. Positive-negative pressure breathing may be helpful under these circumstances.

Stroke volume. Diminution of stroke volume, particularly when accompanied by bradycardia, is a manifestation of decreased ventricular filling during diastole as a result of the fall in venous return to the heart. Therefore, the extent to which ventricular stroke volume is diminished during spinal anaesthesia is related to the height of the sympathetic block and the position of the patient. The reduction in left ventricular stroke volume which accompanies high spinal anaesthesia and which is usually associated with low systemic arterial pressure is quantitatively less than that which occurs when an equal degree of hypotension follows blood loss and peripheral vasoconstriction. In each case the diminution of venous return to the heart is approximately the same, but spinal anaesthesia causes bradycardia, while the others cause tachycardia. Since diastole is shortened during tachycardia, the volume of blood in the ventricles at the start of systole (that is, potential stroke volume) is less during tachycardia than during bradycardia.

Myocardial power and ventricular force. The power of the heart is decreased during spinal anaesthesia. This reduction varies directly with the height of anaesthesia, and is caused by the reduction in peripheral resistance—the pressure against which the ventricle must force blood during systole—and a decrease in stroke volume.

The force of contraction of the myocardium (inotropic effect) is affected by spinal anaesthesia in three ways: decreased ventricular filling—according to Starling's Law the reduced end-diastolic blood volume is associated with a corresponding decrease in the force of myocardial contraction; sympathetic paralysis, involving fibres to the adrenal glands, may lower the catechol amine blood level—which is the potent endogenous positive inotropic substance and contributes to the force of myocardial contraction; and paralysis of the sympathetic cardiac accelerator nerves, which reduces further the force of contraction.

Myocardial irritability. Specific investigations have not been carried out, but spinal anaesthesia possibly reduces irritability because it reduces the blood level of catechol amines.

Coronary blood flow. Although the rate and volume of blood flow through the coronary arteries depend mainly upon mean aortic pressure and secondarily upon myocardial oxygen requirements, coronary flow probably also has self-regulating mechanisms which dilate or constrict the vessels in order to provide the metabolic needs of the myocardium. These changes may be independent of the mean aortic blood pressure.

It has been shown that coronary blood flow decreases during high spinal anaesthesia. This fall is not the same in extent as the fall in mean aortic blood pressure and the oxygen requirements of the myocardium. The coronary flow, therefore, remains quite adequate, provided that the vessels are free from atheromatous plaques and other pathological changes which might initiate thrombosis and myocardial infarction.

Remember. Even though depression of the arterial blood pressure during spinal anaesthesia varies mainly with the height of the sympathetic block (peripheral dilatation) and with cardiac output, the amount of trauma and manipulation to

which a patient is subjected after induction of anaesthesia, and certain constitional factors such as hypertension, old age, hypovolaemia, and pregnancy, also play an important role. In addition, when hypovolaemia is due to active bleeding, the induction of spinal anaesthesia may accelerate the loss of blood by producing vasodilatation in the bleeding area.

Summary. Spinal anaesthesia may have three circulatory effects: decrease of the total of peripheral resistance by interruption of vasoconstrictor impulses to arterioles; pooling of blood in venous circulation, secondary to the post-arteriolar dilatation which reduces venous return to the heart; and decrease in cardiac output due to slowing of the heart rate.

Diethyl Ether (17–20)

In spite of the many undesirable effects of diethyl ether, this agent is still the most widely used in clinical anaesthesia. As a primary agent its effect on the heart becomes an important consideration only in the elderly, the debilitated, and those with metabolic disturbances. Of all the potent general anaesthetic agents, it causes the least respiratory depression for a corresponding level of hypnosis, analgesia, and muscular relaxation. Herein lies its safety (Fig. 3).

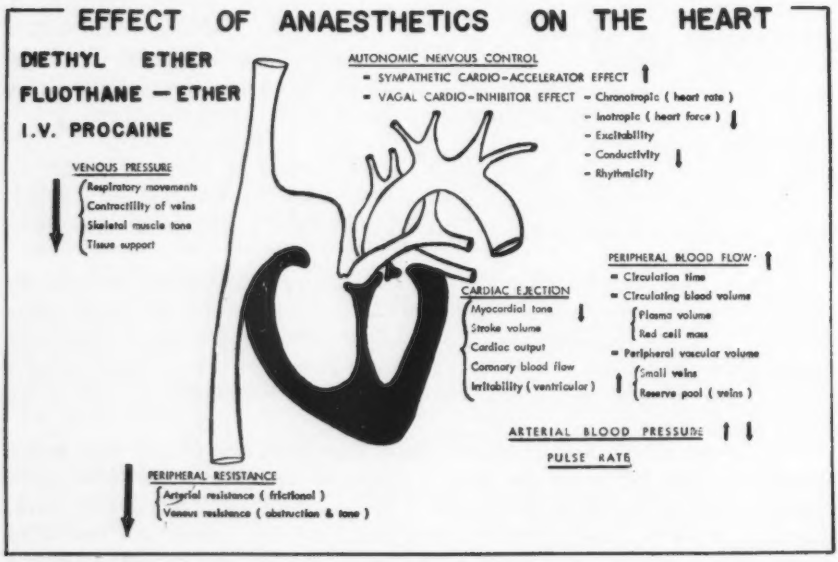

Figure 3

Pulse rate usually increases slightly owing to paresis of the vagal inhibitory mechanism, augmentation of cardiosympathetic impulses, and liberation of norepinephrine and epinephrine.

Arterial blood pressure rises slightly. There is also a widening of the pulse pressure during light planes of anaesthesia, probably for the same reason that the pulse rate rises. However, with increasing depth of anaesthesia, or with prolonged anaesthesia, the blood pressure falls gradually until respiratory depression becomes marked, and then the fall becomes steep.

Cardiac output rises initially in response to the positive inotropic effect of released epinephrine and norepinephrine. As anaesthesia is prolonged, this sympathetic response is exhausted and the depressant effect of ether on the heart becomes dominant. Cardiac output and cardiac power then diminish independently of the depth of anaesthesia. During deep ether anaesthesia there is also a progressive rise in central venous pressure, which probably indicates increasing depression of myocardial tone, that results in a reduction in the stroke volumn.

Peripheral resistance falls progressively with increasing depth of anaesthesia.

ECG. Heart block and ectopic beats are rare during light ether anaesthesia, but as narcosis becomes very deep, they may begin to appear. Arrhythmias due to ether anaesthesia are exceedingly uncommon in humans, and the heart is very resistant to abnormal excitation by catechol amines.

Most laboratory data indicate that ether is a myocardial depressant, but in man the sympathetic stimulation or liberation of catechol amines produces a positive inotropic effect on the heart that overcomes the depressant influence of ether on the myocardium if the patient is healthy.

Cyclopropane (21–26)

The main difference between ether and cyclopropane lies in the severe respiratory depression that surgical depths of anaesthesia produce with the latter. When adequate artificial respiration is provided, the cyclopropane content of the blood can be increased to a level of about 20 per cent above that necessary to produce respiratory arrest without affecting the human heart. At higher concentrations, cyclopropane has a direct myocardial effect which causes serious arrhythmias and heart failure (Fig. 4).

The effects of cyclopropane on haemodynamics are complicated because it has both sympathomimetic and parasympathomimetic properties. A direct sympathomimetic effect or response to release of norepinephrine appears evident from increases in pulmonary artery pressure, central venous pressure, and total peripheral resistance. The slowing of the heart rate may be a parasympathetic response, which is increased by morphine premedication.

Cyclopropane has less effect on the peripherial circulation than have the other potent agents. For this reason it is considered by most anaesthetists to be the best agent to use on patients in compensated or frank shock, particularly that due to acute blood loss and intestinal obstruction.

Pulse rate is slowed slightly below resting levels, but the effect on the heart rate is not striking. Low pulse rates which are seen have been attributed to a pulse deficit due to ectopic beats. The slowing of the pulse rate therefore is not necessarily a sign of increasing depth.

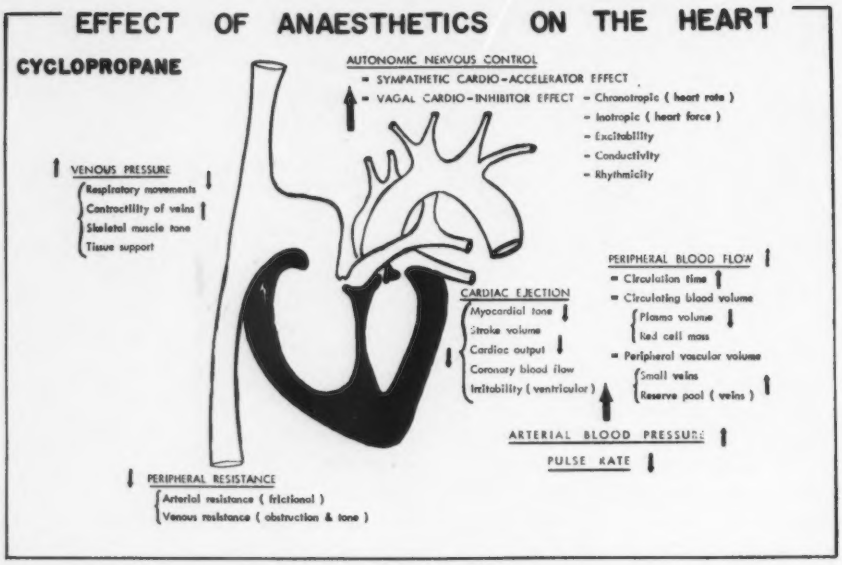

FIGURE 4

Blood pressure. There is no significant alteration in blood pressure during surgical planes of cyclopropane anaesthesia if pulmonary ventilation is adequate. Hypertension that occurs is probably due mainly to the effect of hypercarbia, and is also due to emergence from deep to light levels of anaesthesia. Sensory stimulation, coughing, and intubation at light levels also cause hypertension.

Hypotension often occurs at the end of a cyclopropane anaesthetic, especially when pulmonary ventilation has been inadequate. The post-anaesthetic hypotension after cyclopropane is often difficult to correct.

Cardiac output. During surgical planes of cyclopropane anaesthesia there is a moderate fall in cardiac output, but peripheral vascular tone remains within normal limits or may be elevated, and central venous pressure may be elevated. The latter is more likely a sign of increased blood flow from the periphery than a sign of myocardial incompetence since patients fare better with cyclopropane during shock and haemorrhage than with the other potent agents.

ECG. A rising pCO_2 in the arterial blood increases the incidence of ectopic beats. Spontaneous arrhymthias are not common when pulmonary ventilation is adequate. When they occur, augmenting respiratory exchange, reducing the concentration of cyclopropane in oxygen, and administering a barbiturate have been used successfully for treatment. The heart becomes extremely irritable when catechol amines are injected during cyclopropane anaesthesia. This may be seen on the electrocardiogram by the progressive appearance of a nodal rhythm and ventricular extrasystoles, ventricular tachycardia, and multifocal ventricular extrasystoles leading to auricular and ventricular fibrillation.

TRICHLORETHYLENE (27, 28, 29, 30)

This agent is very toxic to the heart when used as a total anaesthetic as cyclopropane is used. It should never be used for major procedures without sufficient supplementation to reduce the concentration required below 1 per cent. When used in a balanced anaesthetic technique with nitrous oxide–oxygen (3:1 or 2:1), meperidine, and muscle relaxants, it provides excellent analgesia and hypnosis, and a very smooth anaesthetic course with less than 0.5 per cent (Fig. 5).

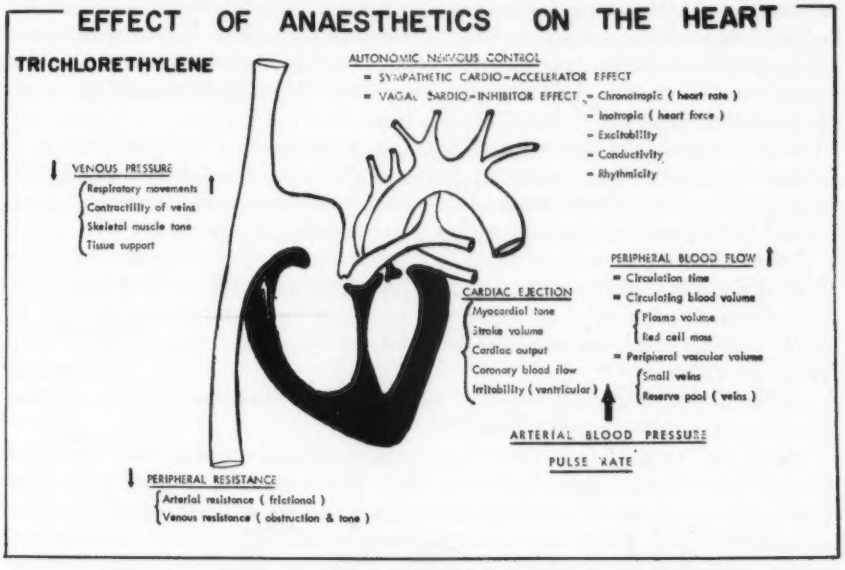

FIGURE 5

In clinical use with supplements, it has little effect on blood pressure or pulse rate, causes moderate peripheral vasodilatation, but even in 1 per cent concentration sensitizes the myocardium to epinephrine. Spontaneous arrhythmias are rarely seen when the concentration is less than 1 per cent, particularly when pulmonary ventilation is augmented. Arrhythmias become common when the concentration exceeds 1.5 per cent, and are seen more than with any other agent if 2 per cent is exceeded, especially if breathing is spontaneous and tachypnoea is allowed to persist.

Ventricular fibrillation with epinephrine is highly likely during anaesthesia with trichlorethylene. For prolonged anaesthesia 0.5 per cent should NOT be exceeded.

CHLOROFORM (31, 32, 33)

The effect of chloroform on the heart is important because cardiac death may occur quickly if it is not administered carefully. It may stop the heart in three ways: by direct myocardial depression, by ventricular fibrillation, and by vagal

inhibition (Fig. 6). When this agent is used for major procedures, an accurately calibrated vaporizer should be employed to control its rate of administration.

Full atropinization combined with a phenothiazine derivative such as perphenazine (5 mg. intramuscularly) or levomepromazine (10 mg. intramuscularly) should be used for premedication, to precede a smooth induction with a sleep dose of thiopental. It is best to use dimethyl d'tubocurarine or succinylcholine to accomplish endotracheal intubation. Thereafter, respiration should be controlled in a non-rebreathing system and anaesthesia maintained with nitrous oxide–oxygen (2:1) and less than 1.5 per cent chloroform for the robust, young, healthy patient and less than 1.0 per cent for the debilitated patient. If muscular relaxation is sometimes not adequate, small doses of a muscle relaxant should be added rather than increasing the concentration of chloroform administered to exceed the above-noted limits.

Blood pressure falls gradually as depth of anaesthesia is increased owing to reduction in peripheral resistance (vasomotor centre depression), myocardial tone and force. The systolic pressure falls more than the diastolic pressure, causing a small pulse pressure when more than 1 per cent is administered.

Pulse rate falls gradually as depth of anaesthesia increases. This slowing of the pulse is a vagal reflex, because atropine prevents or reverts it. With prolonged anaesthesia, the slowing of the pulse may no longer be vagal, but rather may be due to a direct effect of chloroform on the heart, or to the indirect effect from a failing circulation.

Cardiac output falls with excessive chloroform anaesthesia owing to the depression of myocardial tone and ventricular force.

Myocardial excitability. Under light chloroform anaesthesia, some patients develop minor cardiac arrhythmias owing to the vagal effect on the heart. The heart is also sensitized to catecholamines, which will cause ventricular fibrillation —especially if pulmonary ventilation is not adequate. The effect of epinephrine on the heart during chloroform anaesthesia is less than that seen with a corresponding surgical plane of anaesthesia with cyclopropane, Fluothane, and trichlorethylene, but it is dangerous nevertheless.

Fluothane (34, 35, 36, 37)

Fluothane has a characteristic action on the heart and circulation which in man lies closer to chloroform than to cyclopropane when used in the concentration required for surgical anaesthesia (0.5 to 1.0 per cent). It is slightly more potent than chloroform in producing cardiovascular depression, but it is slightly less potent as a hypnotic.

Blood pressure depression is related to the rate and concentration used. When administered slowly from an accurately controlled vaporizer in less than 1 per cent concentration, severe hypotension can usually be avoided. During maintenance of anaesthesia, the blood pressure usually rises somewhat above the induction level but remains below the control level. Hypotension is more likely to occur with muscle relaxants such as d'tubocurarine that with gallamine or succinylcholine.

Pulse rate is usually lowered, but marked bradycardia is not common, and can often be eliminated by full atropinization. As with cyclopropane, there may be a pulse deficit due to ectopic heart beats.

Peripheral blood flow is increased markedly, while peripheral resistance is only slightly reduced.

Ventricular force is reduced as the depth of anaesthesia is increased. The slight reduction in peripheral resistance and marked reduction in myocardial power result in a fall in cardiac output.

Myocardial irritability. Fluothane anaesthesia has a predominant vagal effect on the heart. This moves the pacemaker from the sino-auricular node to the atrioventricular node when excessive depth of anaesthesia or inadequate ventilation is permitted. Depression of the sino-auricular node results in discharges from ectopic centres and a nodal rhythm appears. Arrhythmias may occur during rapid induction and during deep anaesthesia, but usually disappear if the concentration of Fluothane is reduced, if ventilation is improved, and if atropine is administered. In experiments with dogs, ventricular fibrillation is easily produced during light Fluothane anaesthesia if epinephrine is injected (Fig. 6).

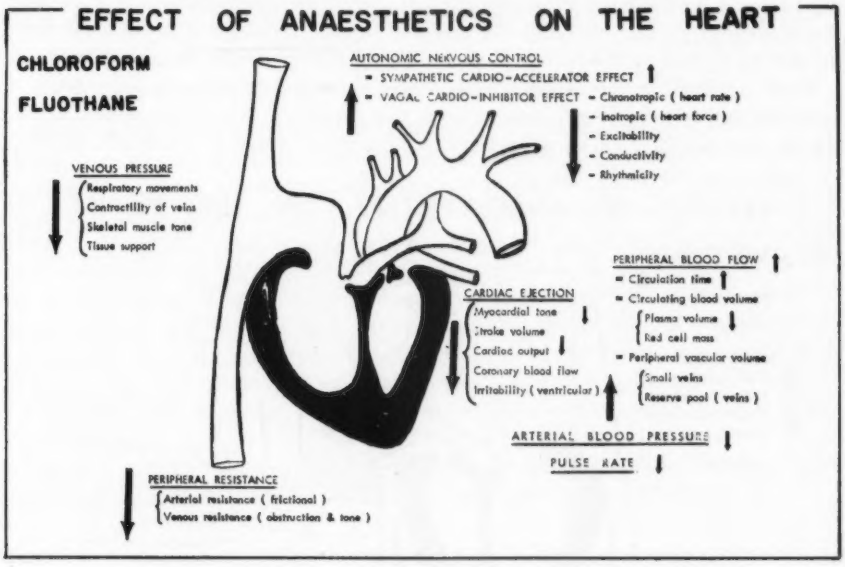

FIGURE 6

FLUOTHANE–ETHER AZEOTROPE (38, 39, 40, 41)

The effect of Fluothane on the heart is reduced significantly when Fluothane–ether azeotrope (68.3 : 31.7 by volume) is employed (Fig. 2). Blood pressure is affected less with a concentration of the mixture that contains more Fluothane than that which might cause marked hypotension. There is less tendency to

slowing of the pulse rate, and the hypotensive response to d'tubocurarine is not seen as frequently. There is moderate reduction in peripheral resistance and in myocardial tone, so that cardiac output does not fall as rapidly with increasing depth of anaesthesia.

Myocardial irritability is also less with the mixture than with Fluothane alone, so that spontaneous arrhythmias are not common if ventilation is adequate, and ventricular fibrillation is far less likely to occur with the injection of epinephrine.

Satisfactory anaesthetic conditions for major operations with little myocardial depression are seen when less than 1.5 per cent of the mixture is used with nitrous oxide–oxygen (2:1) and a muscle relaxant in a non-rebreathing system and with augmented respiration.

Intravenous Barbiturates (42, 43, 44)

The pre-anaesthetic state of the myocardium and peripheral circulation is an important factor in the clinical response to intravenous barbiturates (thiopental, thiamylal, hexobarbital, methitural, buthalitone, methohexital). They have a potentially powerful depressant effect on the myocardium, as indicated by experiments on the heart-lung preparation. However, when given with care, and supplemented by nitrous oxide–oxygen and muscle relaxants, they are no more depressing to the cardiovascular system than ether or cyclopropane (Fig. 7).

Blood pressure. Rapid injection of a large dose of barbiturates may cause a profound fall in arterial pressure. This is due mainly to peripheral vasodilation, loss of peripheral venous tone, reduction of venous return to the heart, pooling

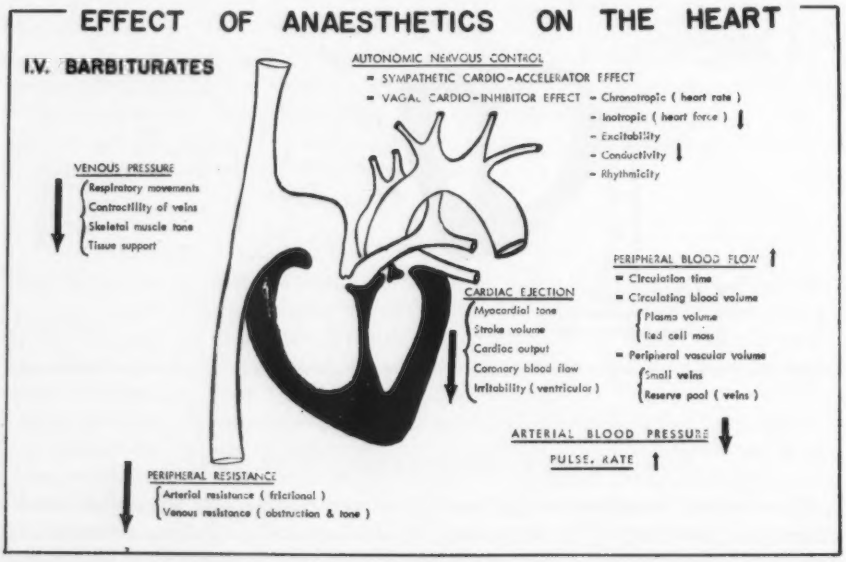

Figure 7

of blood in relaxed peripheral veins, and fall in cardiac output. These may be due to a direct toxic effect on the myocardium—which impairs contractility of the heart. The patient with an impaired myocardium has a greater fall in blood pressure than does a fit person. Any pre-existing coronary insufficiency is increased by the myocardial hypoxia following hypotension, and further decreases the efficiency of the heart muscle.

Patients with hypertension are more likely to have a marked fall in blood pressure. Peripheral vasoconstriction on account of haemorrhage is also lost very quickly with barbiturates, causing profound hypotension. When peripheral vascular tone is already reduced by ganglionic blocking drugs or other vasodilator drugs, the hypotensive effect of barbiturates is exaggerated. Severe hypotension is more likely in elderly patients if the upright posture is adopted. Patients who are "vagotonic" or have a labile blood pressure are also more likely to have a sharp fall in blood pressure with barbiturates.

When artificial respiration with adequate oxygen is provided, very much larger doses of barbiturates are well tolerated.

ECG. Barbiturates are rarely the primary cause of cardiac arrhythmias. Occasionally, ventricular arrhythmias are reported. These may occur if ventilation is inadequate, and the heart becomes hypoxic.

Procaine, Lidocaine, and Related Esters (45, 46, 47)

When administered intravenously, procaine, lidocaine, and their related esters have an action on the heart which is similar to that of quinidine. They are protoplasmic poisons which manifest their action on the heart by depressing the conductivity in the ventricles as well as the atrioventricular node and the auricles. They prolong the refractory period and decrease the excitability of the sino-auricular node and the myocardium, thereby slowing the heart rate. The slowing is not accompanied by an improved capacity of the heart to contract, as is seen with digitalis, but renders the heart less excitable to stimuli and retards the rate of conduction of normal impulses. Large doses also reduce the contractility of the heart, and may cause severe hypotension. Lidocaine causes less vasomotor depression than procaine when used as an intravenous supplement to general anaesthesia.

ECG. Procaine prolongs the PR interval and QRS complex. Excessive doses may cause premature beats, tachycardia, and ventricular fibrillation.

Effect of Narcotic Analgesics on the Heart (48, 49)

When narcotic analgesics (morphine, meperidine, alphaprodine, dipipanone HCl) are administered intravenously in therapeutic doses, there is probably a very mild depressant effect on the healthy heart. The change in circulatory dynamics is related mainly to the general physical condition of the patient and to the rate, concentration, and dose administered (Fig. 8).

Blood pressure. Hypotension may occur immediately after an intravenous injection, probably because of peripheral vasodilatation (direct action on the

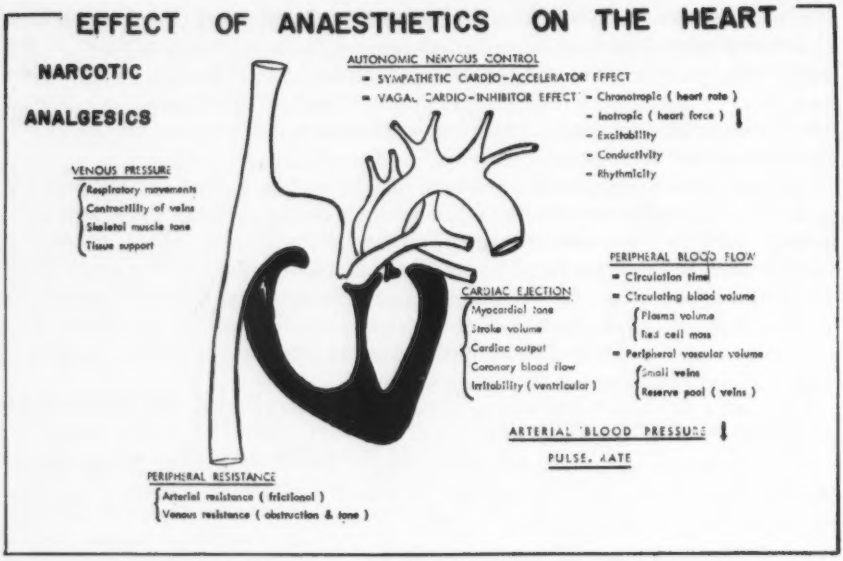

FIGURE 8

vessels), by central vasomotor depression, and perhaps by ganglionic blockade. In the healthy subject, blood pressure is rapidly restored, but in debilitated patients hypotension may persist if it is not treated.

Pulse rate decreases momentarily after meperidine. This may be followed by tachycardia which is prolonged. This is said to be due to its vagolytic action. Morphine may cause slight bradycardia.

Myocardial contractility as measured by strain gauge arch experiments show a brief decrease, followed by a moderate increase in contractility accompanying the period of hypotension with meperidine.

MUSCLE RELAXANTS (50, 51, 52)

These drugs have no significant direct effect on the heart. However, d'tubocurarine may cause some ganglionic block which is seen best when a large dose is injected rapidly during anaesthesia. This will cause hypotension. Flaxedil apparently produces a selective block of the vagus, which results in tachycardia, without change in the blood pressure. Succinylcholine in relatively large doses frequently causes severe bradycardia in infants and young children, which may be reversed with atropine.

PHENOTHIAZINE DERIVATIVES (53, 54)

The main cardiovascular effects of the parenteral administration of most of the phenothiazine derivatives (for example, chlorpromazine) are similar in many

ways to the effect of a high spinal anaesthetic, in which sufficient dilution of the local anaesthetic agent was employed to produce only light sensory anaesthesia. There is a decrease in peripheral vascular resistance which results in hypotension and tachycardia. These may be increased or decreased by posturing. Peripheral blood flow is increased two to four times with chlorpromazine.

The ECG may show an intial sinus arrhythmia, which disappears after a short while.

Myocardial irritability and automaticity are reduced, and there is a greatly reduced positive inotropic response to epinephrine and other vasopressors. Phenothiazines protect the heart against ventricular fibrillation due to epinephrine with chloroform, cyclopropane, trichlorethylene, Fluothane and Fluothane–ether when administered beforehand.

Cardiac output is not reduced by the phenothiazines unless very marked hypotension is produced by the head-up posture. Coronary blood flow is increased by chlorpromazine.

Hypothermia (55, 56, 57)

The effect on the heart of moderate total body cooling (28 to 30° C.) is still the subject of extensive study. Myocardial function is depressed by lowered temperature, but the depression is not the same as that associated with the response to anaesthetic or narcotic drugs (Fig. 9).

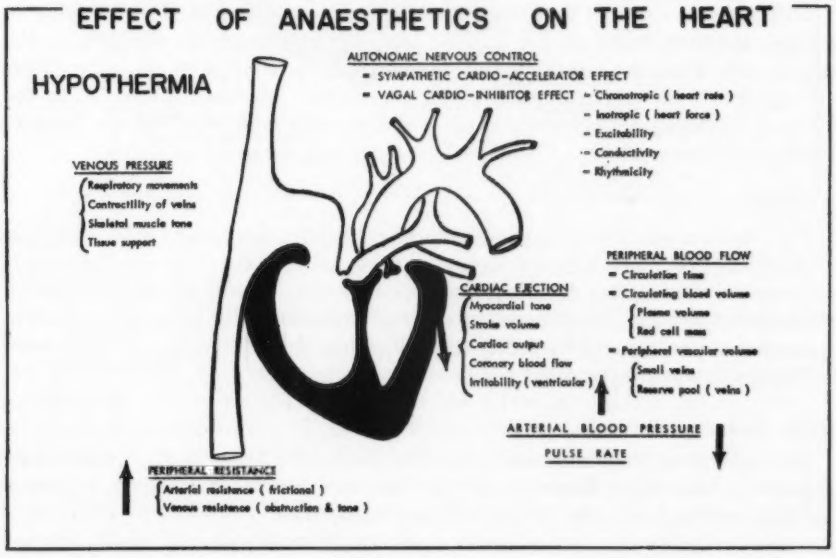

Figure 9

Drug depression implies that myocardial contractility is altered. It is more gradual, the amplitude is lower, the duration is shorter and the stroke volume is reduced. There is also an elevated end-diastolic ventricular pressure. During total

body cooling the only changes in heart action are the more gradual contraction and the lowered amplitude of contraction.

Blood pressure falls slowly during cooling after an initial elevation that is caused by intense vasoconstriction.

Pulse (*heart*) *rate* slows to a greater degree than the fall in blood pressure. The bradycardia induced by cooling the heart differs from that caused by vagal stimulation in that the absolute duration of systole and isometric relaxation increase by 250 to 300 per cent, during hypothermia, whereas systole increases only 50 per cent and isometric relaxation does not change at all with vagal slowing.

Stroke volume remains close to the normal, coronary blood flow and oxygen uptake appear to remain adequate, while cardiac output and work of the heart are reduced during hypothermia.

If the body temperature is allowed to fall below 28° C., the myocardium becomes very irritable and ventricular fibrillation is likely, even when oxygenation and carbon dioxide elimination are satisfactory.

Other Factors Associated with Anaesthesia that Affect the Heart (58–61)

Hypoxia

Mild hypoxia of short duration causes an increase in the heart force owing to reflexes mediated through the carotid body and sympathetic effectors in the spinal cord. When the carotid body or spinal cord (up to C_2) is blocked, the effects of hypoxia on the heart are very much augmented, causing a sharp fall in the force of myocardial contraction, and if the hypoxic condition persists, cardiac standstill follows quickly.

Acidosis

The effects of metabolic and respiratory acidosis are not usually evident during anaesthesia, but they may be added to those of hypoxia. The cardiac output decreases as hypercarbia develops, but the output may be restored to normal with the catechol amines. The depressant effect of acidosis on the heart is due mainly to the fall in pH, because buffering the pH back to 7.40 in the presence of hypercarbia restores the myocardial force.

Heart Disease

The maximum work that can be performed by the heart at any given filling pressure is decreased substantially by the stress of body trauma, hypoxia, acidosis, and especially by disease of the myocardium.

Induced Hypotension (62, 63)

The main result of induced hypotension is the creation of a disparity between the circulating blood volume and the capacity of the vascular bed. The effect on the heart of such a change depends more upon the physical condition of the

patient, the areas which are rendered ischaemic, and the duration of ischaemia, than on the absolute blood pressure at heart level, regardless of the method used to lower the blood pressure (arteriotomy, total spinal block, postural, ganglion-blocking drugs, etc.). In general, a blood pressure that is less than 80 mm. Hg at heart level is critical to the adequate perfusion of the vital organs, and should not exceed a time limit that is related especially to the known recovery time for normal function of the brain, heart, spinal cord, kidney, and liver (Fig. 10).

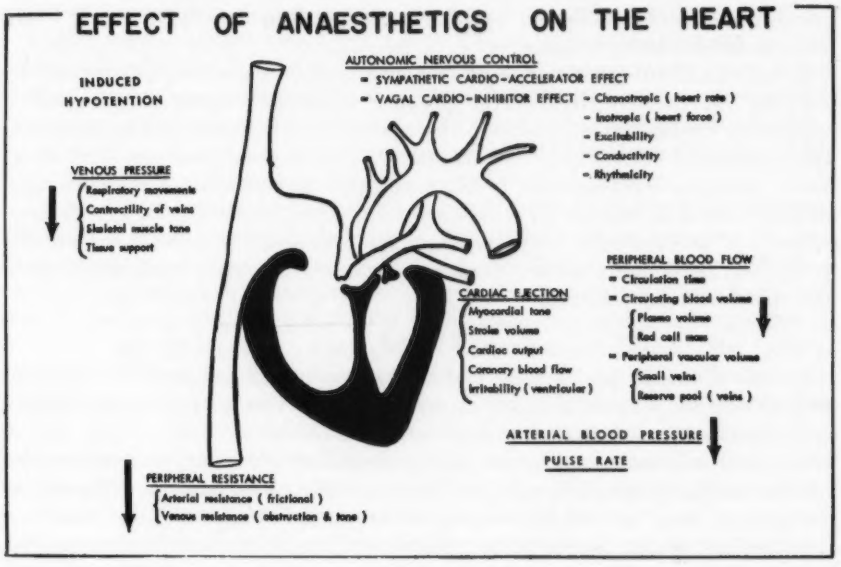

FIGURE 10

Airway Pressure (64–73)

The circulatory effect of positive pressure in the airway has been known for almost a century. Detailed studies have been carried out by many in recent years, and all have shown that whenever air, anaesthetic gases, or vapours are forced into the lungs, there is interference with the circulation if the mean airway pressure is permitted to rise. This interference is especially marked when the patient has a reduced circulating blood volume. The least disturbance of circulation during artificial respiration is achieved when the positive pressure phase is less than one-third of the breathing cycle. During the expiration phase of the breathing cycle, the airway pressure must drop to zero or sub-atmospheric pressure to compensate for the circulatory impedance which occurred during inspiration. The degree of circulatory embarrassment occurring with intermittent positive pressure is determined by the magnitude of the mean airway pressure and the duration of the inspiratory phase.

Abnormal Cardiac Rhythms (74–82)

Abnormal cardiac rhythms may develop during anaesthesia. They are usually caused by a direct effect of the drug on the heart, which may shorten the refractory period, depress the resting electrical potential, or alter the secretion of endogenous substances (for example, catechol amines). Hypoxia, hypercarbia, elevated blood potassium, and a variety of external stimuli also cause abnormal cardiac rhythms. Stimulation or traction of the lung hilus, ribs, stomach, incision of a diseased pleura or pericardium, mechanical pressure on the vagus nerve or carotid sinus, and handling or rotating a diseased heart are particularly likely to cause serious arrhythmias.

In general, most spontaneous arrhythmias may be prevented or reverted by reducing the concentration of the primary anaesthetic agent and increasing pulmonary ventilation to eliminate the possibility of hypoxia and hypercarbia. The addition of ether vapour is very helpful with cyclopropane and with Fluothane. Atropine intravenously to block efferents and procaine locally to block afferents are also helpful. In some cases, quinidine, procaine amide, chlorpromazine, or perphenazine may be given intravenously to depress myocardial irritability, particularly for the treatment of paroxysmal ventricular tachycardia and ventricular extrasystoles.

Résumé

Le rôle principal du cœur est celui d'une pompe unidirectionnelle. Environ 80% du courant sanguin qui passe au cœur est dirigé vers quatre organes vitaux: le cerveau, le foie, le rein et le muscle cardiaque.

On ne peut mesurer la fonction cardiaque qu'indirectement, en mesurant les résistances que le cœur doit vaincre. Parmi ces résistances, il faut mentionner: la viscosité du sang qui modifie le courant sanguin, l'extensibilité des vaisseaux sanguins qui change la résistance périphérique et, enfin, l'inertie du sang qui influence la contractilité du myocarde. Toutes ces résistances sont influencées par l'anesthésie: d'abord, l'hématocrite augmente (la viscosité augmente), l'extensibilité diminue (la résistance périphérique diminue) et la contraction du myocarde diminue (le débit systolique et le débit cardiaque diminuent).

Une autre conception importante en anesthésie est la relation entre la résistance artérielle et la résistance veineuse. Les modifications de cette relation ne sont pas sans influencer la pression de perfusion du cerveau, du cœur, et du rein et, plus spécialement, au cours de l'anesthésie profonde, durant l'hypothermie et l'hypotension provoquée avec l'emploi d'agents ganglioplégiques. Lorsque la résistance artérielle augmente, la pression artérielle s'élève sans grande modification du débit cardiaque; par contre, lorsque la résistance veineuse augmente, la pression artérielle et le débit cardiaque tombent à pic. D'autre part, une augmentation proportionnelle des deux résistances: artérielle et veineuse n'abaisse pas la pression artérielle, mais le débit cardiaque subit une légère diminution.

Lorsque les parois vasculaires sont normales, la résistance préartériolaire compte pour environ 5 à 15% de la pression aortique. Au cours d'une hémorragie et d'une anesthésie profonde, la résistance préartériolaire augmente et peut compter jusqu'à 50% de la pression aortique. Dans ces éventualités, le cœur

emploie la moitié de son énergie pour pousser le sang dans les artérioles. La perfusion tissulaire devient alors considérablement réduite.

Quels sont les effets spécifiques des agents anesthésiques sur le coeur?

Il est difficile d'être positif sur la sécurité relative d'un agent anesthésique en tenant compte de son action sur le cœur parce que cette sécurité tient davantage à l'habileté avec laquelle l'agent est donné ainsi qu'aux mesures thérapeutiques que l'anesthésiste prudent emploie qu'aux propriétés inhérentes de n'importe quel agent anesthésique.

L'effet cardiovasculaire de tout agent dépend principalement de sa voie d'administration, de sa vitesse d'injection et de sa concentration selon que le malade respire spontanément ou que sa ventilation est augmentée, selon la profondeur et la durée de l'anesthésie et selon l'état physique général du malade—en attachant une importance spéciale à la fonction cardiopulmonaire préanesthésique et au volume du sang circulant.

L'effet des agents anesthésiques sur l'hémodynamique demeure spécialement difficile à préciser à cause du fait que la circulation normale engendre toujours des réflexes circulatoires et apporte dans la circulation des substances endogènes sécrétées en réponse à l'injection des poisons. Chacun agit sur une partie différente de la dynamique circulatoire pour éviter un changement général. Il s'impose, en conséquence, d'enregistrer simultanément autant de facteurs variables que possible. Ces facteurs variables nous procurent des indices plus fiables dans tout le cadre affecté et le sens des changements. *Il est rarement possible de tirer des conclusions sur les mécanismes des effets circulatoires d'un médicament à la suite des changements qu'il peut produire sur un seul facteur variable tel le débit cardiaque.* Pour ce qui concerne l'hémodynamique, tous les paramètres cardiorespiratoires devraient être enrégistrés.

C'est encore la mesure directe de la tension artérielle qui, comme seule mesure, demeure la plus importante parce que:

(*a*) Le débit ventriculaire droit, en définitive, peut être apprécié par le débit ventriculaire gauche et la tension artérielle, ce qui donne une idée du retour veineux.

(*b*) Les effets circulatoires, en général, apparaissent précocement sur la tension artérielle.

(*c*) On peut y suivre les réponses instantanées de battement en battement.

Il existe certains effets spécifiques reconnus que chaque agent produit sur le cœur—ou bien directement sur sa force de contraction et sur son excitabilité ou bien indirectement en libérant des hormones endogènes–épinéphrine, norepinéphrine, acetylcholine, histamine ou serotonine; ou encore en changeant le tonus veineux périphérique qui affecte le retour du sang au cœur; ou encore en déprimant la respiration, ce qui entraîne de l'hypoxie myocardique et de l'acidose.

En général, toute dépression respiratoire par un agent anesthésique entraine d'abord une augmentation de la force de contraction du myocarde—suivie après d'une diminution progressive. Cette diminution progressive de la force de contraction du myocarde accompagne habituellement l'approfondissement de l'anesthésie chirurgicale, peu importe l'agent employé. L'état de vasoconstriction

observé avant l'induction de l'anesthésie fait place rapidement à une augmentation du volume de sang circulant périphérique à mesure que s'approfondit l'anesthésie. Cela s'accompagne également d'une diminution du volume de sang circulant dans les principaux organes de l'organisme. Quand il existe des pathologies cardiaques, tous les changements cardiovasculaires causés par l'anesthésie sont aggravés.

La rachianesthésie agit sur le cœur de trois façons à cause de la paralysie des fibres sympathiques vasomotrices au niveau préganglionnaire. Il se produit d'abord une diminution de la résistance périphérique totale par interruption des influx vasoconstricteurs aux artérioles; il s'ensuit une accumulation de sang dans la circulation veineuse, conséquence de la dilatation postartériolaire, ce qui diminue le retour veineux au cœur; enfin, le débit cardiaque diminue à cause du ralentissement du cœur.

L'éther diéthylique n'a pas d'effet marqué sur le cœur normal parce qu'une libération de catécholamines, dès le début, maintient l'homéostase cardiovasculaire. Si l'on recourt à de l'anesthésie profonde ou prolongée, il se produit une dépression progressive du myocarde et de la circulation périphérique.

Le cyclopropane agit beaucoup moins sur la circulation périphérique que l'éther diéthylique et il exerce peu d'effet dépresseur sur le cœur si la ventilation pulmonaire est maintenue adéquate. Toutefois, le cyclopropane est très irritant pour le système de conduction du cœur et il entraîne des arythmies sérieuses durant l'anesthésie profonde ou si des catécholamines entrent en circulation. Le trichlorethylène est également très irritant pour le cœur; il ne devrait pas être employé comme agent anesthésique primaire sans avoir une source d'atmosphère suffisante pour réduire la concentration inhalée à moins de 1%. Le chloroforme et le Fluothane peuvent également agir sérieusement sur la fonction cardiaque en produisant directement une dépression myocardique par stimulation vagale et par de sérieuses arythmies ventriculaires lorsque des catécholamines entrent en circulation. Si ces substances anesthésiques sont employées en faible concentration avec une ventilation assistée et que le malade reçoit des doses thérapeutiques d'atropine, elles n'ont pas d'effets sérieux sur le cœur. Le mélange azéotropique Fluothane–éther produit sur le cœur des effets semblables à ceux du Fluothane et du chloroforme mais ces effets sont beaucoup moins marqués. La procaïne et la Xylocaïne dépriment la conduction dans le myocarde de façon semblable à celle de la quinidine et ils rendent le cœur moins sensible aux stimuli. De grandes doses de ces médicaments réduisent la force de contraction du myocarde et peuvent entraîner une hypotension marquée.

Les barbituriques intraveineux ont peu d'effets dépresseurs sur le cœur normal et sur la circulation périphérique à moins qu'on les administre rapidement ou à fortes doses. On peut affirmer la même chose des narcotiques analgésiques et des myorésolutifs qu'on administre par les veines. Les dérivés puissants du phénothiazine n'exerce que peu d'effet direct sur le cœur mais ils agissent sur la circulation en diminuant le tonus vasculaire périphérique, produisant de l'hypotension, de la tachycardie et une augmentation du volume de sang circulant périphérique.

Il existe d'autres facteurs qui, s'ils sont ajoutés à l'anesthésie, agissent sur le cœur de la façon suivante:

L'hypothermie légère produit une diminution plus graduelle et plus marquée de l'amplitude de contraction du cœur. Cela diffère de la dépression médicamenteuse qui raccourcit également la durée de la contraction et entraîne une élévation de la pression ventriculaire à la fin de la diastole. Une hypothermie plus prononcée augmente l'irritabilité myocardique au point de conduire à la fibrillation ventriculaire.

Une hypoxie légère et de courte durée augmente la contractilité myocardique. Pour peu qu'elle se prolonge, surtout s'il existe une dépression sympathique, la contractilité myocardique diminue très rapidement.

L'acidose (respiratoire et/ou métabolique) diminue la contractilité myocardique à cause de l'abaissement du pH. S'il existe des pathologies cardiaques, les effets dépresseurs de l'hypoxie et de l'acidose sont beaucoup plus manifestes.

L'hypotension provoquée entraîne un écart entre le colume de sang circulant et la capacité du lit vasculaire. Cela n'affecte pas le cœur si le retour veineux est augmenté et si la pression sanguine n'est pas abaissée au-dessous du niveau de la pression de perfusion nécessaire requise par les organes vitaux.

Une élévation de la pression moyenne de l'atmosphère produite en augmentant la ventilation durant l'anesthésie déprime la fonction cardiaque en retardant le retour du sang veineux. Les effets dépresseurs sur le cœur sont d'autant plus marqués que le malade possède un volume de sang circulant réduit.

Au cours de l'anesthésie, on peut observer des rythmes anormaux. Ils s'observent habituellement à la suite de l'effet direct de certains médicaments sur le cœur, médicaments qui peuvent raccourcir la période réfractaire, déprimer le potentiel électrique de repos ou encore modifier la sécrétion de substances endogènes qui affectent le cœur (e.g., catécholamines). L'hypoxie, l'hypercarbie, un taux de potassium sanguin élevé et une variété de stimuli externes peuvent également conduire à des rythmes cardiaques anormaux. Une stimulation ou une traction sur les hiles, les côtes, l'estomac, l'incision d'une plèvre malade, du péricarde, une pression mécanique sur le vague ou sur le sinus carotidien ou encore la manipulation ou la rotation d'un cœur malade, tous ces gestes sont susceptibles de produire de sérieuses arythmies.

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OBSTRUCTION OF THE AIRWAY IN THE NEWBORN BY ASPIRATION OF FOETAL MEMBRANE: A CASE REPORT

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OBSTRUCTION OF THE AIRWAY in the newborn infant by aspiration of foetal membrane has not previously been reported in the literature as far as we can determine.

CASE REPORT

A woman, para ii, gravida iv, was admitted to hospital in well-established labour with a breech presentation. Labour had progressed normally to full dilatation of the cervix when the foetal heart sounds disappeared. Examination showed a prolapsed loop of cord. The patient was immediately anaesthetized with nitrous oxide/trichlorethylene/oxygen, with the addition of succinylcholine chloride 40 mg., for relaxation, and delivery was completed with the utmost despatch, ventilation being maintained throughout by intermittent positive pressure.

FIGURE 1

On delivery the baby was limp and pale, and no cardiac pulsation was evident. Blood and amniotic fluid were aspirated from the pharynx under direct vision, and immediate intubation of the trachea was done with a Mann's metal tube

(1). Brief suction was applied to the endotracheal tube, and an attempt was made to inflate the lungs with oxygen. The lungs failing to inflate, suction was again applied to the tube and it was withdrawn. A long string of membrane was found impacted into the distal end of the tube. The tube was cleared and reinserted, when the lungs inflated with ease with the Mann Resuscitator (12 cm. H_2O pressure). The infant did not survive.

The membrane removed from the trachea measured 5×7 cm. (Fig. 1). Pathological examination confirmed that it was foetal membrane.

En autant que nous sachions, il n'a jamais été rapporté dans la littérature de cas d'obstruction des voies respiratoires chez le nouveau-né par l'aspiration de membrane fœtale.

Histoire du cas

Une femme, para ii, gravida iv, est entré à l'hôpital en travail avec une présentation du siège. Le travail avait été normal jusqu'à la dilatation complète du col, alors que les bruits du cœur fœtal disparurent. L'examen a révélé une procidence du cordon. On a immédiatement soumis la malade à une anesthésie générale avec du protoxide/chloroéthylène/oxygène en ajoutant de la succinylcholine 40 mg. pour obtenir du relâchement et l'accouchement a été complété avec célérité, en assurant une ventilation adéquate par une pression positive intermittente.

Après la délivrance, le bébé était flasque et pâle et on ne percevait pas de pulsation. Sous vision directe, nous avons aspiré du liquide amniotique dans le pharynx et nous avons pratiqué une intubation trachéale avec un tube métallique de Mann. Nous avons pratiqué un peu de succion sur le tube endotrachéal et nous avons essayé d'insuffler les poumons de l'enfant avec de l'oxygène. Comme les poumons ne pouvaient être gonflés, nous avons appliqué de nouveau la succion sur le tube endotrachéal et nous l'avons retiré. Un long filet de membrane obstruait le bout distal du tube. Le tube a été nettoyé et remis en place et les poumons, avec facilité cette fois, ont pu être gonflés avec le resuscitateur de Mann (12 cm., H_2O de pression). Malheureusement l'enfant n'a pas survécu.

La membrane enlevée de la trachée mesurait 5×7 cm. (Fig. 1). La pathologie a confirmé qu'il s'agissait de membrane fœtale.

REFERENCE

1. Mann, J. Resuscitation of the Newborn: A Method and a Machine. Anesth. & Analg. *33*: 289 (Sept.–Oct., 1954).

AN ADAPTATION OF THE HEIDBRINK TRICHLORETHYLENE CIRCUIT FOR PAEDIATRIC ETHER ANAESTHESIA

A. J. DUNN, M.D.[1]

THIS MODIFICATION of the Heidbrink trichlorethylene circuit for ether anaesthesia was devised to meet the requests of some of our surgeons that endotracheal methods be made available for tonsillectomy patients of all ages.

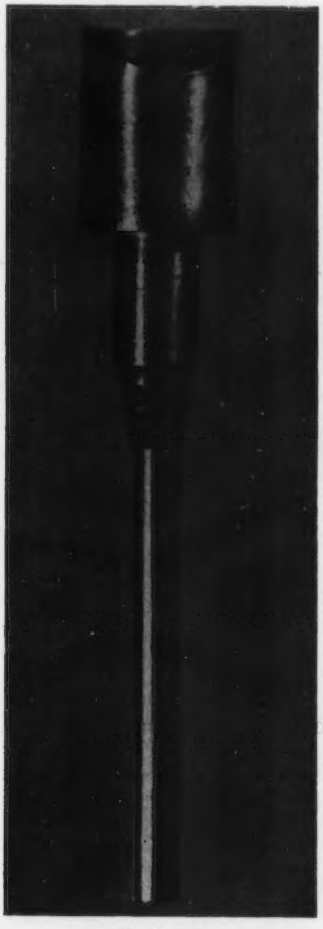

FIGURE 1

[1]Department of Anaesthesia, St. Michael's Hospital, Toronto, Ont.

Equipment

The only non-standard apparatus needed is that shown in Figure 1. This pipe, used for bubbling oxygen and nitrous oxide through the Heidbrink ether bottle, was made from a discarded yoke-fitting endotracheal connector, to which was soldered a length of copper tubing, of 3/8 in. internal diameter to reach to 1/2 in. from the bottom of the bottle (Fig. 2). This pipe, which fits the gas inlet

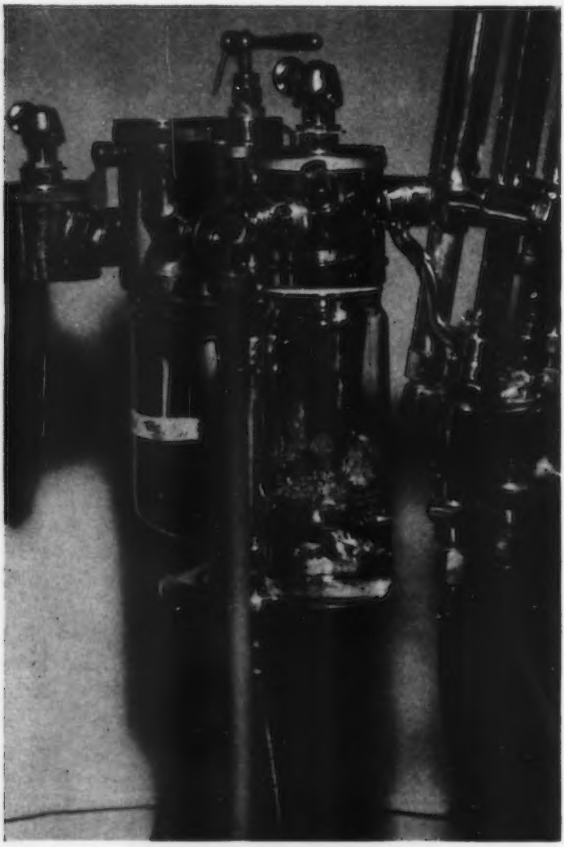

Figure 2

of the bottle, is unsuitable for the closed-circuit ether bottle, where the pipe which accommodates it is the ether vapour outlet. Gases and ether vapour are conducted to the patient through a length of rubber tubing, which is connected to a reservoir bag and non-rebreathing valve, with a catheter mount, as shown in Figure 3. The endotracheal connector is held to the mouth gag by a blunted towel clip. The headrest shown in Figure 4 combines lateral fixation with a scapular rest, which eliminates the need for manual hyperextension of the child's

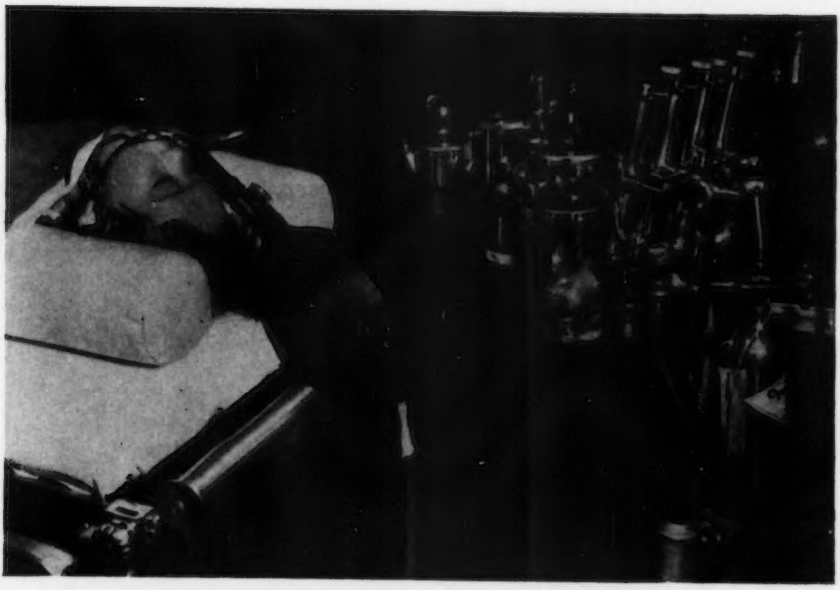

FIGURE 3

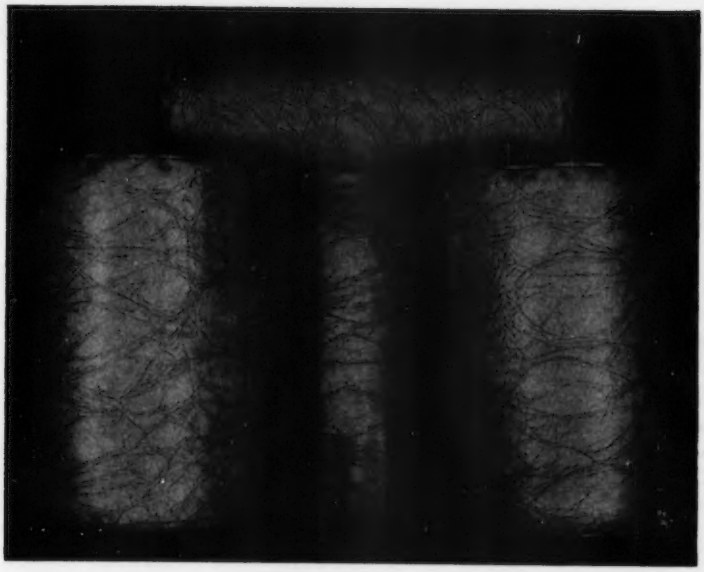

FIGURE 4

neck, and keeps the pharynx dependent. An alternative arrangement for eye surgery is shown in Figure 5. Here the reservoir bag is kept at the bottle outlet, so that there is no interference with draping. In this picture may be seen the water-jacket, made from a suture jar, which maintains a more constant vapour concentration in longer eye procedures.

FIGURE 5

TECHNIQUE

Anaesthesia is induced in atropinized, unsedated children by ethyl chloride and ether, and the child is intubated without relaxant, and connected to the reservoir bag. From this point on, anaesthetic depth is controlled by:

1. Varying the lever setting at a constant gas flow to cause more bubbling
2. Varying the total gas flow, at a constant lever setting, above minute volume needs
3. Varying the N_2O/O_2 ratio
4. Use of the water-jacket.

This apparatus is capable of producing deep anaesthesia very quickly; so a minimal rate of bubbling should be aimed at, that will maintain a quiet operative field. In many cases, ether can be discontinued after one tonsil has been removed, and N_2O and O_2 will suffice for the rest of the operation. The water-jacket is usually unnecessary for tonsillectomy, unless the surgeon is against intubation. In this case, the reservoir bag and valve are replaced by an ether hook, and the water-jacket gives a higher vapour concentration, and prevents frosting of the

bottle at higher rates of bubbling. Dead space can be minimized for small children with endotracheal tubes, by shortening the catheter mount until the valve and connector are in contact.

Advantages

As Percheson and Carroll have said (1), endotracheal intubation is the *sine qua non* of good paediatric anaesthesia. It is indispensable to the proper use of the non-rebreathing, Ayre's, and relaxant methods. This apparatus frees the hands of the anaesthetist to do the major part of the operation, which he is usually required to do. It places the reservoir bag in the field of vision of the anaesthetist, so that pupillary and respiratory signs are always available. It eliminates the semi-obstructed airway so common with open methods. It allows an oxygen-rich atmosphere to be inhaled, so that dark blood need never be seen in the operative field. Anaesthesia can be conducted at a lighter level with an endotracheal tube in place, so that reflexes usually return before the child leaves the theatre. The apparatus is removable, so that the machine may be used for non-explosive anaesthesia.

Disadvantages

Laryngitis and tracheitis are possible, but have not been seen in the author's cases. The tube causes slight restriction of the operative field, to which the surgeon soon adapts.

Summary and Conclusions

A flexible, controllable method of endotracheal ether anaesthesia for children has been described, using a simple modification of the Heidbrink trichlorethylene circuit. This has proven safe and satisfactory in over 200 cases, of ½ to 2 hours duration, with no complications due to the method.

Acknowledgments

I wish to thank Dr. T. Molony, who designed the head cushion shown, and Mr. A. Smialowski, for the photography.

Résumé

Nous avons décrit une technique d'anesthésie pédiatrique à l'éther, technique flexible, contrôlable, endotrachéale, en modifiant simplement le circuit à trichlorethylène Heidbrink. Cette façon de procéder s'est avérée de toute sécurité et satisfaisante au cours de 200 cas, d'une durée variant de ½ heure à 2 heures, et nous n'avons observé aucune complication attribuable à cette méthode.

REFERENCE

1. Percheson & Carroll. Difficulties in Paediatric Anaesthesia. Canad. Anaesth. Soc. J. *5*: 115 (April, 1958).

L'ANESTHESISTE DOIT ETRE PRATIQUE ET ECONOME

LEON LONGTIN, M.D.

SI, à votre avis, les tubes corrugués que vous employez sur votre machine à anesthésie ne remplissent plus adéquatement leur fonction essentielle, ne les jetez pas, ils peuvent encore remplir une fonction secondaire: ils peuvent servir à fabriquer des coussins pour tenir la tête de vos malades, plus particulièrement les enfants.

Les principaux avantages de ces anneaux ou "beignes" faits avec les tubes corrugués usagés en comparaison avec ceux qui sont faits en tissu ou autrement sont les suivants: (i) ils sont conducteurs; (ii) ils sont pneumatiques; (iii) ils sont lavables; (iv) on les fait en peu de temps et sans difficulté; (v) ils ne coûtent rien. Voilà qui est pratique et économique!

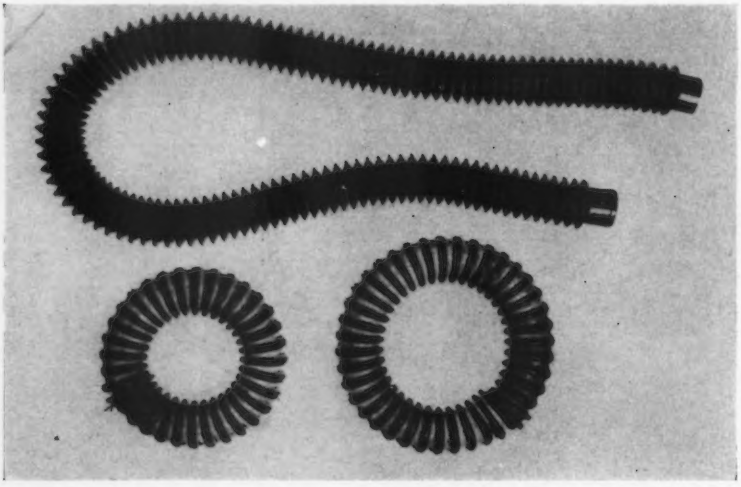

FIGURE 1

OBITUARY

Beverly Charles Leech

The death of Dr. Beverly Charles Leech occurred in Nanaimo, B.C., on March 10, 1960, following a cerebral-vascular accident. "Bev" Leech was born in Brandon, Man., on May 9, 1898, and received his preliminary education at Central Collegiate, Regina, Sask., and Brandon College, Brandon. Following service in the C.E.F. in World War I, where he attained the rank of lieutenant in the infantry, he returned to Canada and entered McGill University, from which he graduated in 1925 with the Degree of M.D., C.M. He established practice in Regina and became Director of Anaesthesia at the Regina General Hospital in 1929, an appointment which he held until 1956. In 1956, he semi-retired to Nanaimo, where he continued practice until his sudden death.

Dr. Leech also served in World War II, with the rank of lieutenant-colonel and later colonel in the R.C.A.M.C., as Officer Commanding the 10th Canadian Field Ambulance, 1939–1942; Officer Commanding No. 5 Canadian General Hospital, 1942–1944; and Assistant Director Medical Services, 2nd Canadian Division, 1944.

Honours, relating to his war service, were many and included the Order of the British Empire, Canadian Efficiency Decoration, Canadian Forces Decoration, and the Legion d'Honneur (France).

Honours bestowed upon Dr. Leech as a specialist in anaesthesia were also many and international, and his associations with anaesthetic societies were numerous: Honorary Fellow of the Association of Anaesthetists of Great Britain and Ireland, 1942; Honorary Member of the Section of Anaesthetists of the Royal Society of Medicine, 1942; Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons, 1950; Charter Member of the American Society of Anesthesiologists, 1937; American Board of Anesthesiology, 1939; Fellow of the International College of Anesthesiologists, 1936; Certified Specialist of the Royal College of Physicians and Surgeons of Canada, Anaesthesia, 1943; Charter Member of the Canadian Anaesthetists' Society, President, 1948–9, and Life Member, 1956; Charter Member of the Anaesthetists' Travel Club, which later became the Academy of Anesthesiology.

A pioneer of Canadian anaesthesia has departed. His many international associations have ended. Those of us who were privileged to know Bev Leech are deeply grieved. He was ever willing to help and sponsor the younger members of his specialty. The Canadian Anaesthetists' Society, the Saskatchewan Division, and the British Columbia Division have lost a distinguished member.

To his widow, Elsie, and son, Beverly, Jr., we offer our sincere sympathy.

H.B.G.

An Appreciation

Bev Leech was one of the historic names in Canadian anaesthesia. At a time when few others were interested, he was a leader in the fields of teaching, research, and medical organization and economics. During the difficult years of the 1930's he stood fast against all the storms which swirled around him and continued to demonstrate that good anaesthesia was one of the fundamental concomitants of good medicine. He was not only a good anaesthetist but also a good doctor and a good citizen.

When the war came in 1939 Bev Leech unhesitatingly offered his services, and served throughout those long years in positions of great stress and responsibility. He returned to more hard work in anaesthesia, and persisted in spite of poor health until he had the satisfaction of seeing the specialty established on a very firm basis throughout Western Canada.

Every Canadian anaesthetist should say a little prayer of thankfulness to God for having given us Bev Leech as a leader.

Harold R. Griffith, M.D.

BOOK REVIEWS

A PRACTICE OF ANAESTHESIA. By W. D. Wylie and H. C. Churchill-Davidson. Chicago: The Year Book Publishers, Inc. 1960. $20.00.

This exceptionally fine textbook presents a study of anaesthesia from the point of view of basic physiology, anatomy, pharmacology, and pathology. The work is well planned and well written. Although one feels that much of the material might be expanded with benefit, the student of the specialty who takes the trouble to use the well-chosen reference list will miss nothing of great importance. This volume is most highly recommended to teachers and students of the specialty.

R.A.G.

GENERAL ANAESTHESIA. By Frankis T. Evans and T. Cecil Gray. Toronto: Butterworth & Co. (Canada) Ltd. 2. vols. $29.50.

One's reaction on being presented with a multiple volume work on Anaesthesia may be that this specialty is getting beyond bounds, but to include all required material in one volume is no longer practical and Drs. Evans and Gray have met this challenge.

This two-volume publication, which replaces *Modern Practice in Anaesthesia* by Frankis T. Evans, is a well-organized series of chapters by over twenty British authorities. The first volume of 531 pages covers the basic principles of anaesthesia, including anatomy, physiology and pharmacology. The material in these basic science subjects is collected from many sources by authors specially qualified to present the anaesthetist with up-to-date information which he would find only with difficulty in journals and texts.

The second volume of 431 pages entitled *Techniques, Special Fields and Hazards* includes, in addition, chapters on immediate postoperative care, respiratory insufficiency, oxygen therapy and the medico-legal aspects of general anaesthesia. Local anaesthesia is not included.

As must be expected with many different authors there is variation in style and concept and some overlap in material. These volumes are well indexed and each chapter carries excellent bibliography and references. The printing and binding are first class and the illustrations and drawings are clear and well done.

S.M.C.

NEWS LETTER

Western Divisions' Meeting

The Annual Meeting of the Western Divisions of the Canadian Anaesthetists' Society was held at the Empress Hotel, Victoria, B.C., from April 27 to 30, 1960. The members of the British Columbia Division were hosts for the meeting. The programme theme was "Hypoxia," and the programme was remarkable for both the quality of the presentations and the calibre of the participants (see this Journal, April, 1960). The hospitality of the B.C. Division was complemented by beautiful spring weather which made it possible for the guests to enjoy the golf, fishing, and sight-seeing arranged by their hosts. Once again the Western Meeting has maintained its reputation as one of the most profitable and most friendly of the year's "conventions."

R.A.G.

The *Calgary Anaesthetists' Society* has been reorganized after a period of inactivity. The Executive for 1960 consists of:

Chairman	Dr. J. H. A. Lawrence
Secretary-Treasurer	Dr. W. M. Jones
Co-ordinator	Dr. W. Johns

Dr. J. Hayakawa of the Department of Anaesthesia of St. Boniface Hospital, Winnipeg, was married to Miss Jane Hook on February 27, 1960.

Dr. H. Camrass has been appointed anaesthetist at the Brandon General Hospital, Brandon, Man.

The programme of the *Winnipeg Anaesthetic Society* during the season 1959–60 consisted of the following:

October, 1959	Azeotropic Fluothane–Ether Anesthesia—Dr. Gordon Wyant
November, 1959	Panel on Chronic Pulmonary Disease and Anaesthesia Chairman—Dr. Max Minuck Panelists—Dr. D. Snidal Dr. P. F. McGarry Dr. G. Ross
January, 1960	Muscle Relaxants—Dr. T. McCaughey, Dr. Mark Nickerson
February, 1960	Medical Films
March, 1960	Presentation of Complications of Anaesthesia
April, 1960	Differential Brain Cooling—Dr. S. Cantor, Dr. W. Zingg
May, 1960	Dr. Robert Smith, Boston, Guest Speaker.

Conférences Anesthésiques de Québec

Les lundis soirs de 7.30 à 9 heures ont lieu dans plusieurs hôpitaux de Québec depuis janvier 1960 les conférences anesthésiques du lundi. Ces travaux scientifiques ont été présentes par quelques anesthésistes et d'autres spécialistes versés dans les sciences de bases qui s'y rapportent. Les sujets traités portaient sur l'anoxie, l'arrêt cardiaque, le transport du CO_2 dans le sang, la physique, la physiologie de l'anoxie, le volume sanguin, l'anesthésie et electroencéphalographie et l'anesthésie en neuro-chirurgie et en chirurgie thoracique.

Ces cours ont été organisés par les anesthésistes de l'Hôpital Laval, de l'Hôpital de l'Enfant-Jésus et de l'Hôpital St. François d'Assise et sont destinés à compléter la formation théorique et pratique que reçoivent les Résidents en Anesthésie dans leurs hôpitaux respectifs.

Les assistances ont été nombreuses et même beaucoup d'anesthésistes de Québec et de la banlieue ont suivi régulièrement ces leçons.

Considérant le succès remporté cette année, les organisateurs préparent une nouvelle çédule de conférences qui seront données au cours de l'année académique 1960–1.

Atlantic Provinces' Meeting

The Second Annual Meeting of the Atlantic Provinces Anaesthetists was held in Moncton, April 22–23. The meeting was enjoyed by the 28 who attended.

Dr. Harold Griffith and Dr. Bart Sutherland of Montreal were the guest speakers. Their papers and discussion added much to the sessions.

A business meeting was held, during which an Atlantic Provinces Anaesthetic Committee was set up. This committee is to study the feasibility and problems of an Atlantic certification standard which could be used by all or any of the four Atlantic provinces to provide a second standard of anaesthetic proficiency.

The Atlantic Provinces Anaesthetic Meeting will again be held in Moncton, April 21–22, 1961.

Executives of Provincial Divisions, 1960–1961

British Columbia

Chairman	Dr. J. Blair Fulton
Vice-Chairman	Dr. W. L. Esdale
Secretary-Treasurer	Dr. G. E. Sleath
Program Committee Chairman	Dr. H. H. Macartney
Economics Committee Chairman	Dr. N. R. J. McMillen
Members at Large	Dr. A. C. Blair
	Dr. J. M. Hiddleston
(Vancouver Island)	Dr. R. G. Whitehead
Ex officio	Dr. R. E. Simpson

Alberta

Chairman	Dr. E. H. Dobbs
Secretary-Treasurer	Dr. N. E. Foster
Councillor	Dr. William Strome

Saskatchewan

Chairman	Dr. D. Ewart
Secretary-Treasurer	Dr. Z. Kubinski

Manitoba

Chairman	Dr. Max Minuck
Vice-Chairman	Dr. J. McCammon
Secretary-Treasurer	Dr. Arnold Holm

Ontario

Chairman	Dr. E. S. Russell
Secretary-Treasurer	Dr. D. W. S. Best
Council	Dr. J. M. Shapley
	Dr. J. M. Wishart
	Dr. G. F. Smith

Quebec

Président et représentant, Section Clinique de Montréal/President and representative, Montreal Clinical Section	Dr. David Power
Président sortant de charge/Past President	Dr. J. P. Déchène
Premier Vice-Président et représentant, Section Clinique du Saguenay/First Vice-President and representative, Saguenay Clinical Section	Dr. Gaston Comtois
Deuxième Vice-President et représentant Section Clinique de Québec/Second Vice-President and representative Quebec Clinical Section	Dr. Paul E. Galibois
Représentants au Conseil/Representatives to Council	Dr. Harold Griffith, Dr. Georges Cousineau
Secrétaire-Trésorier/Secretary-Treasurer	Dr. Guy Fortin
Assistant Secrétaire-Trésorier/Assistant Secretary-Treasurer	Dr. Gérard Migneault
Représentants Universitaires/University Representatives	
Montreal	Dr. Léon Longtin
McGill	Dr. Richard G. B. Gilbert
Laval	Dr. Fernando Hudon
Représentant Collège des Médecins et Chirurgiens, Province de Québec/Representative College of Physicians and Surgeons, Province of Quebec	Dr. Roger Gagnon
Représentants des Sections Cliniques/Representatives Clinical Sections	
Cantons de l'Est/Eastern Townships	Dr. Patrick Laughrea
Bas St-Laurent/Lower St. Lawrence	Dr. Paul Plourde
Saint-Maurice/Saint Maurice	Dr. Marc Allen
Outaouais et Nord-Ouest du Québec/Ottawa Valley and North Western Quebec	Dr. Richard Lemieux
Montreal	Dr. Louis H. Gatien, Dr. John B. Sutherland

New Brunswick

Chairman	Dr. E. Daigle
Secretary-Treasurer	Dr. J. Arthur Dobson

Nova Scotia

Chairman	Dr. C. H. L. Baker
Secretary-Treasurer	Dr. Ian E. Purkis

Prince Edward Island

Chairman	Dr. L. E. Prowse

Newfoundland

President	Dr. C. D. Kean
Secretary-Treasurer	Dr. T. G. Stentaford
Member of Council	Dr. T. G. Stentaford
Member of Economics Committee	Dr. C. U. Henderson

SECOND WORLD CONGRESS OF ANAESTHESIOLOGISTS
DEUXIÈME CONGRÈS MONDIAL DES ANESTHÉSISTES

FORM C **FORMULE C**

APPLICATION FOR ENROLMENT
DEMANDE D'INSCRIPTION COMME MEMBRE

TO:
A: The Manager,
Second World Congress of Anaesthesiologists,
2 College St.,
Toronto 5, Ontario, Canada.

I wish to enrol as an active member of the Second World Congress of Anaesthesiologists, to be held in Toronto, Ontario, Canada, September 4th to 10th, 1960.

Je désire m'inscrire comme membre actif du Deuxième Congrès Mondial des Anesthésistes, qui aura lieu à Toronto, Ontario, Canada, du 4 au 10 septembre, 1960.

PLEASE PRINT IN BLOCK LETTERS — EN CAPITALES D'IMPRIMERIE, S'IL VOUS PLAIT

SURNAME
NOM .....

CHRISTIAN OR GIVEN NAMES
PRENOMS .....

ADDRESS
ADRESSE .....

.....

.....

ACADEMIC APPOINTMENT OR AFFILIATION
SITUATION ACADÉMIQUE OU ASSOCIATION .....

LANGUAGE PREFERENCE
LANGUE CHOISIE .....

Are you attending as the representative of any Government, Society or Organization? If so, please specify .....

Participez-vous comme représentant d'un Gouvernement, d'une société ou d'une organisation quelconque? Si oui, veuillez préciser .....

I shall be accompanied by the following associate members
Je serai accompagné par les membres associés suivants .....

.....

(Names) (Noms)

FEES: Active Membership: $25.00 Canadian payable before March 31, 1960, or $30.00 if submitted after March 31, 1960.

Associate Membership: $10.00 Canadian payable before March 31, 1960, or $15.00 if submitted after March 31, 1960.

I enclose money order or bank draft for $..... payable in Canadian funds.

Enrolment fees will be returned to those unable to attend the Congress who so notify the Manager prior to August 1, 1960.

DROITS D'INSCRIPTION: Membre Actif: Dollars canadiens $25.00 à toucher avant le 31 mars, 1960; $30.00 si présenté après le 31 mars, 1960.

Ci-joint un mandat ou un chèque pour $..... payable en dollars canadiens.

Les droits d'inscription seront remboursés à ceux qui ne pourront pas assister au Congrès, et qui en avertiront l'Organisateur avant le 1er août 1960.

Date .....

NOTE: Forms for requesting hotel accommodations will be sent at a later date to all who return this form.

Signature .....

NOTE: Les formes pour les réservations d'hôtel seront envoyées plus tard aux personnes qui auront retourné cette forme.

SEGUNDO CONGRESO MUNDIAL DE ANESTESIOLÓGOS
ZWEITER WELTKONGRESS DER ANAESTHESIOLOGEN

FORMA C **FORMULAR C**

SOLICITUD DE PERMISO PARA PARTICIPAR EN EL CONGRESO
ANMELDUNG ZUR TEILNAHME

DIRIGIDA A:

AN: The Manager,
Second World Congress of Anaesthesiologists,
2 College St.,
Toronto 5, Ontario, Canada.

Deseo registrarme como miembro activo del Segundo Congreso Internacional de Anestesiológos que tendrá lugar en Toronto, Ontario, Canadá, desde el día 4 hasta el día 10 de septiembre de 1960.

Ich wünsche als aktives Mitglied am zweiten Weltkongress der Anaesthesiologen teilzunehmen, der vom 4. bis 10. September 1960 in Toronto, Ontario, Canada, stattfinden wird.

HÁGASE EL FAVOR DE IMPRIMIR EN MAYÚSCULAS — BITTE IN DRUCKSCHRIFT AUSZUFÜLLEN

APELLIDO
FAMILIENNAME .....

NOMBRE DE BAUTISMO O DE PILA
VORNAME(N) .....

DIRECCIÓN POSTAL
ADRESSE .....

DESIGNACIÓN O AFILIACIÓN ACADÉMICA
AKADEMISCHE STELLUNG ODER BEZIEHUNG .....

IDIOMA PREFERIDO EN EXPRESARSE
BEVORZUGTE SPRACHE .....

¿Piensa usted asistir en capacidad de representante de un gobierno, una sociedad u organización? En caso afirmativo, tenga la bondad de especificarse.
Nehmen Sie als Vertreter einer Regierung, Vereinigung oder Organisation teil? Im Bejahungsfalle bitte um genaue Angabe.

.....

Los siguientes colegas me acompañarán .....

.....

(Nombres)

Ich werde von den folgenden Mitgliedern begleitet werden .....

.....

(Namen)

CUOTAS:

Miembro activo: $25.00 (moneda canadiense) pagaderos antes del 31 de marzo de 1960, o $30.00 (moneda canadiense) entregados después del 31 de marzo de 1960.

Miembro asociado: $10.00 (moneda canadiense) pagaderos antes del 31 de marzo de 1960, a $15.00 (moneda canadiense) entragados después del 31 de marzo de 1960.

Adjunto letra de cambio o giro en $..... pagaderos en moneda canadiense.

Los gastos de matrícula seran reembolsados á todos aquellos que se vean incapacitados de atender al Congreso, siempre que asi se lo notifiquen al Director del Congreso antes del primero de agosto de 1960.

Fechada en
Datum .....

NOTA: Más tarde se mandarán formularios para acomodaciones de hotel, a quienes devuelvan esta hoja.

GEBÜHREN: Für aktive Mitglieder— $25.00 (kanad.) zahlbar vor dem 31 März, 1960 oder $30.00 (kanad.) überwiesen dem 31 März, 1960.

Für teilnehmende Mitglieder— $10.00 (kanad.) zahlbar vor dem 31 März, 1960 oder $15.00 (kanad.) überwiesen nach dem 31 März, 1960.

Beiliegend Postüberweisung oder Bankwechsel für $..... zahlbar in kanadischer Währung.

Anmeldegebühren werden im Falle einer Verhinderung der Teilnahme am Kongress zurückerstattet, wenn die Kongressleitung vor dem 1. August 1960 hiervon benachrichtigt wird.

Firma
Unterschrift .....

ANMERKUNG: Formulare zur Anforderung von Hotelzimmern werden später an alle Einsender dieses Formulars versandt werden.

NOTICE

RESIDENTS IN ANAESTHESIA

The Organizing Committee for the Second World Congress of Anaesthesiologists of the World Federation of Societies of Anaesthesiologists has arranged a

SPECIAL CONGRESS REGISTRATION FEE FOR RESIDENTS IN ANAESTHESIA

This fee is $10.00 (Canadian) and should be forwarded to the following address:

Manager
Second World Congress of Anaesthesiologists
2 College St.
Toronto 2, Ontario, Canada

The Registration must be accompanied by a certificate in the following form signed by the Chief of the Department of Anaesthesia in which the Resident is training:

To: *Second World Congress of Anaesthesiologists*

I hereby certify that .....
(*Name*)

is a Resident in training in Anaesthesia, and entitled to the benefit of the special registration fee for Residents attending the Congress.

..... M..D
(*Signature*)

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NOTICE TO USERS OF MARK 1 (3% maximum) FLUOTECS

A few instances have occurred where an early Mark 1 Fluotec could have delivered an unexpectedly high concentration. A modification has been made which prevents this possibility.

The purpose of this notice is to explain:

(1) How the possibility may occur in Mark 1 Fluotecs.

(2) How the modification prevents this possibility.

(3) The procedure to be adopted by users of Mark 1 Fluotecs in order to have them modified.

Inspection of the diagrammatic drawing Fig. 1 will show that the concentration delivered depends on the relative opening of the thermostat H and the diluting valve G.

The valve G is attached to a spindle F. This spindle F is screwed into the cylindrical block R on which is cut the spiral. Turning the dial rotates the spiral and adjusts the amount of opening of the diluting valve G.

The correct opening of the valve G was set in our works by analysis of the issuing gases and when this was correct the spindle was locked to the block R, by a set screw S, which forms a conical indentation, or crater, in the spindle by pressure.

In the few cases mentioned, this screw has become loose and rotated enough to clear the crater. If this happens, the opening of the valve G will no longer correspond to the position of the dial M, and the concentration delivered may be too high or too low.

The Mark 2 Fluotec has three set screws of a larger size than in Mark 1, and they are additionally locked with shellac, so that even if they should loosen, they cannot rotate and so break out of their craters.

Fluotecs now being issued have a modified design of diluting valve and the serial number of this type is followed by the letter A.

In the A modification, this problem has been attacked in two ways:

(1) The block R is now fixed to the spindle by a stout pin passing through both block and spindle. The whole is then soldered.

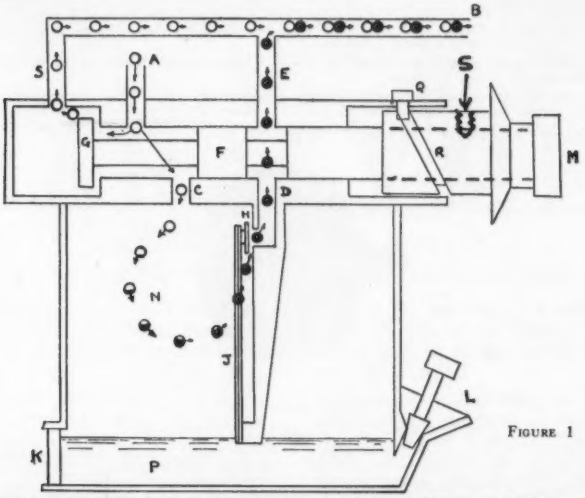


FIGURE 1

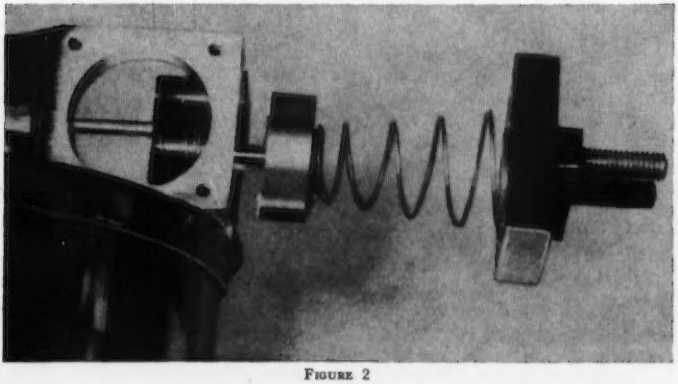


FIGURE 2

(2) In the Mark 1, a rich mixture can be caused if the diluting valve comes nearer to the valve seat than its original setting position. It follows that if it could be arranged that when the valve is touching its seat a sufficient orifice is left to give the required maximum percentage, this percentage could not be exceeded. This has been done by machining two steps on the valve, the depth of which is adjusted at our works to give the correct gap for the maximum percentage shown on the dial (Fig. 2 and 3). Therefore, when the dial is at maximum, the steps of the valve are held on the seat and the gap cannot become smaller. On the rotation of the dial to weaker percentages the valve is pushed off its seat by the spiral in the usual way.

Fortunately, this modification can easily be applied to existing Fluotecs and we are anxious to convert all Mark 1 Fluotecs to this design as soon as practicable and at no charge.

The work involved in converting all Mark 1 Fluotecs is considerable and we think the following plan will cause the least delay.

(1) Any Mark 1 Fluotec with the letter A after the serial number has already been converted and need not be sent back.

(2) Any Mark 1 Fluotec, serial number between 1 and 200 (in the United States and Canada serial numbers 1000—1050), should be returned to us as soon as possible for modification.

(3) If you have any Mark 1 Fluotecs of higher serial number than 200 (in the United States and Canada serial numbers over 1050), please fill in their serial numbers on the enclosed card and return it to us. We will then inform you when to send them in for modification.

(4) If you have a Fluotec of a higher serial number than 200 (in the United States and Canada serial numbers over 1050) and wish to continue using it, the following tests should be applied to see that the block R is firmly attached to the spindle F (Fig. 1).

(A) Remove any plug fitting from the outlet. The spindle with its attached diluting valve can then be seen (Fig. 4). If necessary, the Fluotec outlet may be removed by taking out the four fixing screws, shown in Fig. 4.

(B) Rotate the dial to maximum and put a scratch or pencil mark on the valve opposite the semi-circular channel in the body.

(C) Place the index finger against the valve and while applying a little pressure to the valve, rotate the dial backwards and forwards a few times.

(D) Return the dial to maximum and note the position of the pencil mark. If the pencil mark has changed position, return the Fluotec to us, whatever its serial number.

(E) With the dial at 1% to 2% insert a 0.008 inch (0.2 millimetre) feeler gauge between the valve and its seat and rotate towards maximum.

(F) If the feeler gauge is gripped before the dial has been rotated to maximum, return the Fluotec to us whatever its serial number.

(G) These simple tests should be repeated if ever doubt should arise. While the Fluotec passes these two tests it will be in order to continue to use it until we can undertake to modify it.

It will assist us very much if you will tie or stick a label on the Fluotec, telling us to whom it should be returned when modified.

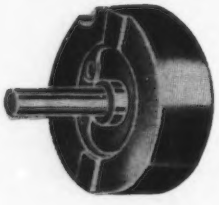
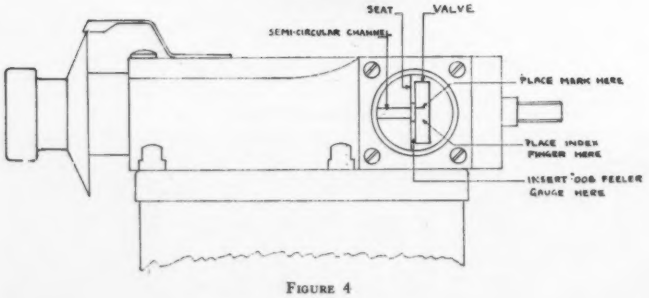


FIGURE 3



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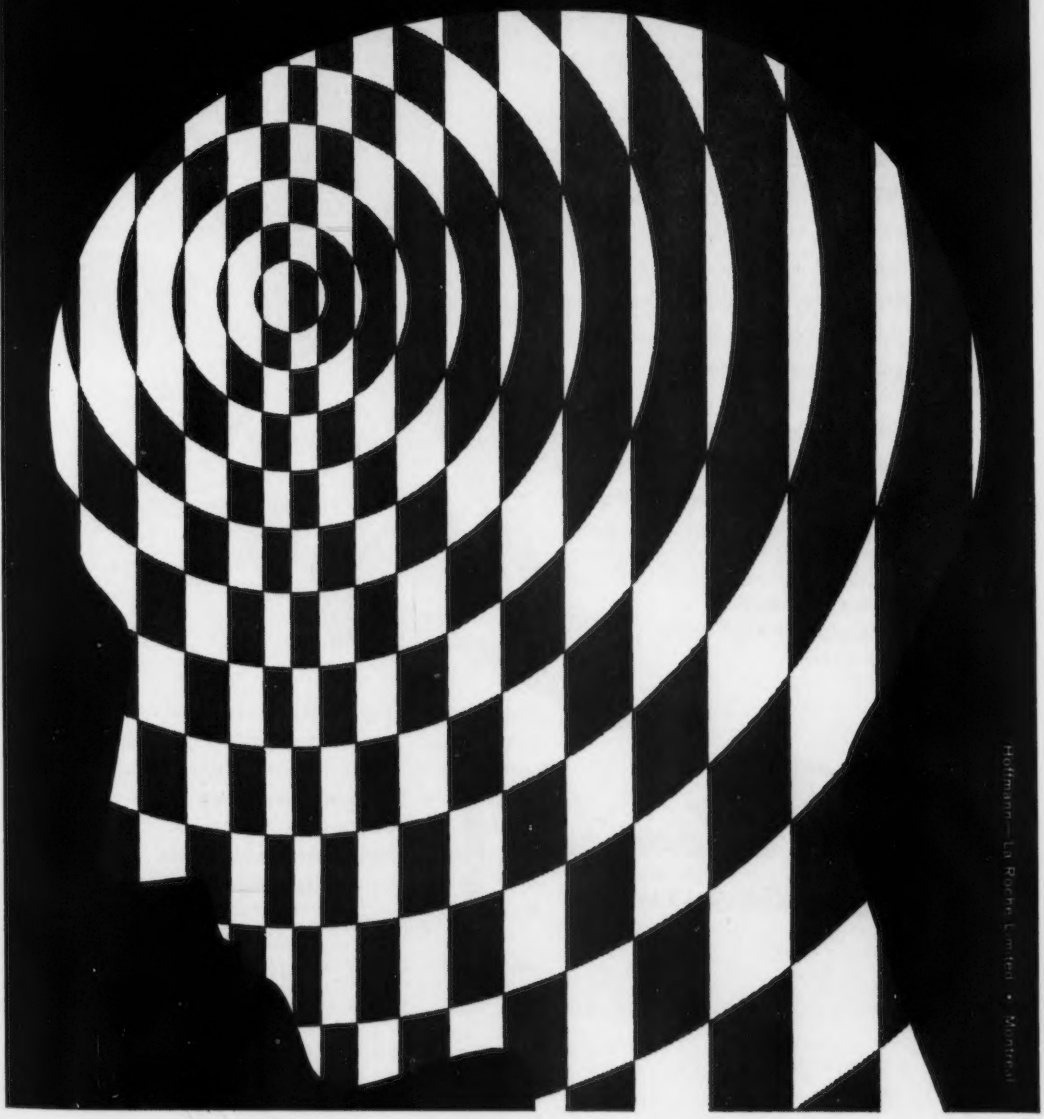

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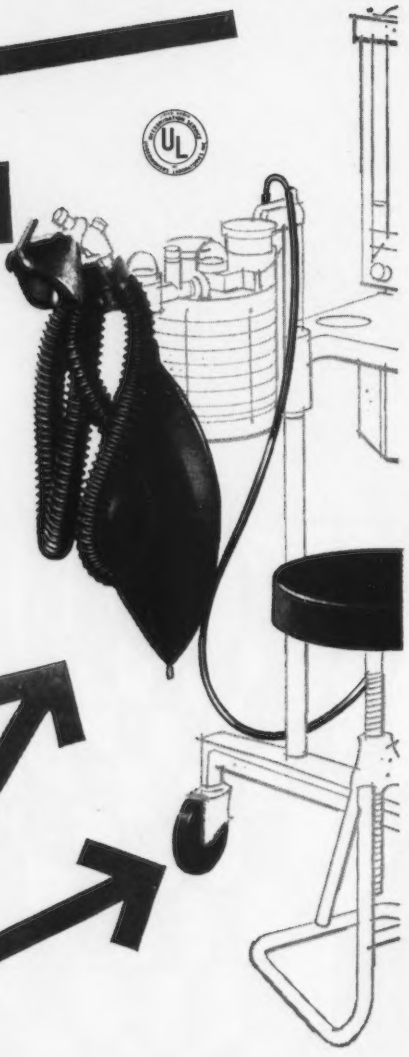

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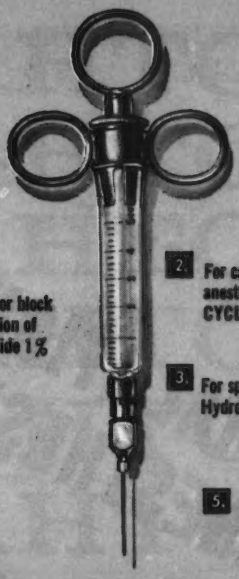

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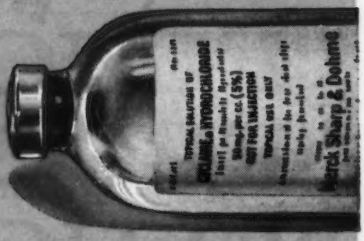

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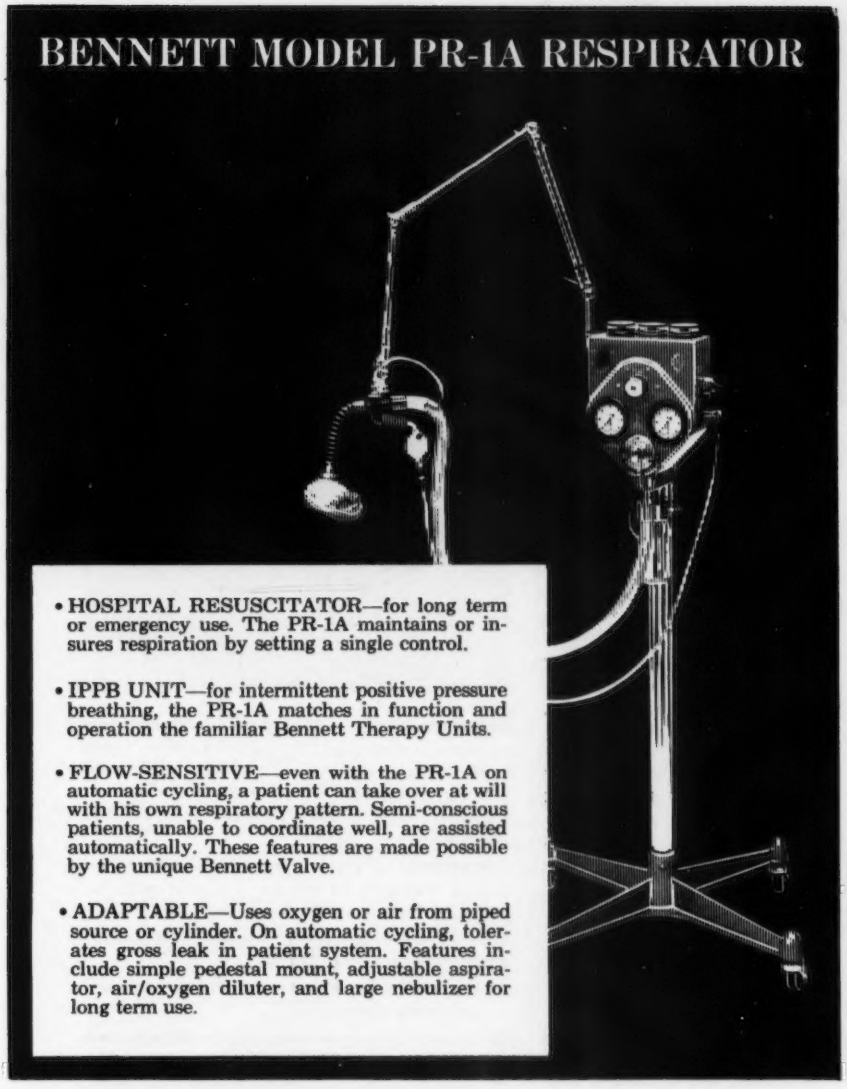

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